ARCHIVES OF SURGERY

VOLUME 30 FEBRUARY 1935 NUMBER 2

ETIOLOGY AND TREATMENT OF CLAWFOOT

REPORT OF THE RESULTS IN ONE HUNDRED AND TWO FEET TREATED BY ANTERIOR TARSAL RESECTION

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The many theories regarding the cause of clawfoot and the wide variety of methods of treatment indicate that the true nature of the deformity is not yet known. Interest in the condition lies in the lure of the unknown, the more so because most of the acquired human deformities have been adequately explained.

Observations on the occurrence, progress and response to treatment of over 400 cases of clawfoot at the New York Orthopaedic Hospital during the past three and one-half years are the basis for this study. The report includes a discussion of the etiology with evidence pointing to the spinal cord as the location of the causative lesion, a review of treatment, and the end-results in 102 feet treated by anterior tarsal resection.

The terms pes cavus, talipes arcuatus, talipes plantaris, hollow or contracted foot, *griffe pied creux, Hohlfuss* and nondeforming clubfoot have been used to designate the deformity.

The typical condition presents an exaggeration in the height of the longitudinal arch with slight shortening of the foot, prominent metatarsal heads, clawing of the toes, loss of flexibility in all the joints of the foot, reduction of treading surface and often a limited dorsal flexion at the ankle joint.

DESCRIPTION

Clawfoot is considered a distinct deformity and differs from paralytic calcaneus or requinus associated with an exaggerated longitudinal arch and from other distortions of the foot resulting from known muscular weakness in that these deformities lack early stiffness of the foot and clawing of the toes. Clawfoot develops most often during adolescence and is about as common in boys as in girls. No relationship with race or social status has been demonstrated.

A mild degree of this condition occurs frequently and is often considered a well formed foot with a high arch rather than a deformity.

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Submitted in January 1934 in partial fulfilment of the requirements for the degree of Doctor of Medical Sciences in the Faculty of Medicine of Columbia University.

The deformity disappears on standing, and it is possible to correct it by applying pressure under the head of the first metatarsal. At a somewhat later stage the high arch becomes obvious and the ball of the foot very prominent; the toes become hyperextended at the metatarsophalangeal joints and flexed at the interphalangeal joints. Dorsal flexion of the foot is usually limited. This limitation may be due to a contracted calf or to a deformity within the foot; usually it is a combination of both factors. In clawfoot of marked degree the cavus becomes very conspicuous and does not disappear on standing. Occasionally flexibility is progressively lost until the foot is almost rigid. The toes become markedly clawed, stiff and, in extreme cases, dislocated dorsally. The width of the foot is increased at the level of the metatarsal heads, and callosities develop under them owing to increased pressure at these points as a result of stiffness and diminished treading surface. The equinus type of deformity is often such as to make it impossible for the patient to stand with the heel touching the floor. There is frequently an associated moderate varus position of the heel and slight adduction deformity of the forefoot.

SYMPTOMS

The symptoms of mild cases are often voiced by the parents, who complain that it is difficult to find comfortable shoes for the child or that shoes become misshapen and wear out quickly. It is not uncommon to find on the dorsum of the foot tender areas resulting from pressure of the shoes. Easy fatigue and weak ankles are frequent complaints. As stiffness and deformity develop the gait becomes ungraceful and jarring, awkwardness is noted, and stumbling occurs.

Callosities appear with the more marked deformity and cause great discomfort. They usually develop under the first and fifth metatarsal heads, and in extreme cases ulcers arise in them. Corns develop early from pressure of the shoes on the knuckles of hammer toes. The friction and pressure against the shoe at these points are increased at each step by the action of the long extensors of the toes in their attempt to assist in dorsal flexion of the foot. Clawfoot may be a most distressing and disabling condition, leading patients to agree to any procedure which promises relief.

HISTORY

Clawfoot with marked equinus deformity is probably the condition described by Andry in 1741 as "bolt feet":

> They hide this deformity by wearing shoes of the ordinary shape, but having that part within which the foot leaves a void, filled up with a bit of cork, or stuffed with flocks . . . it is not absolutely incurable; but it may be helped if not cured by pulling frequently, but very gently, the toes of the child.

The treatment advocated by Andry, in addition to prescriptions for soaking the foot in tripe broth and for rubbing the calves with oil of worms, consisted of replacing wooden heels by lead and advising stretching of the calves by mountain climbing.

In the middle of the nineteenth century clawfoot was confused with, and described as, a variety of congenital and acquired clubfoot. Little (1853) described it as a separate condition. He suggested rheumatic inflammation as its cause and used tenotomies in treatment. Barwell (1865) included a description of clawfoot in his book "On the Cure of Clubfoot Without Cutting Tendons." He thought that the cause was a weak muscle in the calf and treated the deformity by using rubber springs to assist this group of muscles. Duchenne (1863) described the action of the intrinsic muscles of the foot and gave as his theory of the production of clawfoot a weakness of the muscles supplied by the lateral plantar nerve. This theory has had a profound influence since its publication and is accepted as the most satisfactory explanation by many authors today. Golding-Bird (1883), in England, could not confirm Duchenne's observations and suggested weak peroneal muscles as the cause of clawfoot. Fisher (1889) also disagreed and contributed to the literature by suggesting transient weakness of the dorsal flexors of the foot, due to childhood fevers, as the etiologic factor. Shaffer (1885) published some interesting observations on infantile paralysis and contributed the term "nondeforming clubfoot." He stated that he had noted quite frequently, as early as 1865, that when both lower extremities had been paralyzed and had apparently entirely recovered, or in some cases in which there was unilateral paralysis, abnormalities appeared in the supposedly sound limb.

The work of recent writers shows a continued endeavor to find an adequate explanation for this deformity as well as some procedure to secure lasting relief. Hoffman (1912) devised an operation for severe grades of clawed toes which consisted of resection of all the metatarsal heads. Forbes (1913) described the difficulties of treatment and advised transplantation of the long toe extensor tendons to the necks of the metatarsals. Steindler (1917) published a description of his well known stripping operation for the release of the plantar fascia. In 1921 he wrote that this procedure alone was not sufficient in many cases and advised resection of bone to correct the cavus deformity. In 1919 Hibbs published his method of transplanting the long toe extensor tendons to the cuneiform bones. Recent European literature has described radical surgical procedures as necessary to assure permanent correction of the deformity. Numerous articles have appeared describing associated spina bifida occulta and thickening of the dura mater of the spinal cord. A comprehensive monograph on clawfoot, with an almost complete bibliography, was published by Hackenbroch (1926).

He recognized the progressive nature of the condition and recommended complete correction of the deformity by resection of bone and by transplantation and lengthening of tendons.

ETIOLOGY

Clawfoot may be associated with many known conditions or may occur without demonstrable cause. The literature contains numerous references to its cause or causes, whereas some authors state that there is no evident etiologic factor. Because he could find no adequate explanation for clawfoot Mills (1924) was drawn to a study of it. He wrote:

> . . . on consulting a standard textbook on orthopaedic surgery I found eight separate causes given for this singularly precise and definite deformity. The impression left on my mind from reading the list was one of surprise that anyone managed to escape the disease. I was also reminded forcibly of the remark of one of my surgical teachers to the effect that, when a number of different forms of treatment were given for one disease, no one of them was satisfactory.

The theories of etiology which are most frequently advanced are discussed later. They are: congenital origin, acute illnesses of childhood, constriction of the feet during growth, intrinsic and extrinsic muscular imbalance, paralysis in the foot following poliomyelitis, diseases of the central nervous system, heredity, trauma and infection.

CONGENITAL ORIGIN

Cases known to be of congenital origin are rare, and few physicians claim to have seen one. The condition is supposed to be due to defective development of the spinal cord or to an imperfect formation of the plantar structures of the foot. Goff (1933) reported a case in a fetus of 7½ months with congenital syphilis. European writers suggest that spina bifida occulta is the cause of the "idiopathic" group of cases. They observe that at birth the spinal cord ends at the level of the third lumbar vertebra, and when adult life is reached, at the first lumbar vertebra. Accordingly they claim that with the growth of the bony canal away from the lower end of the spinal cord and the presence of congenital adhesions, traction is exerted on the nerve structures. A case with spontaneous correction of the deformity in the foot following laminectomy in a patient with spina bifida occulta was reported by Kochs (1927). Spina bifida or other congenital abnormalities which involve the spinal cord have been described as the cause of clubfoot as well as of clawfoot. In his book, "Congenital Club-Foot," Brockman (1933) stated that clubfoot and spina bifida, when occurring together, are not interdependent but coincident. He referred to the work of Parker and Shattock (1884), who showed that in these cases nerves and muscles, when examined macroscopically and microscopically, exhibited nothing abnormal. He also referred to Harrison (1904),

who demonstrated that muscle fibers developed independently of the influence of the nervous system. Duncher (1913) stated that occult spina bifida was present in 80 per cent of his cases of clawfoot. At this hospital spina bifida occulta has been found to occur incidentally in 20 per cent of patients with scoliosis, none of whom had obvious clawfoot deformity.

ACUTE ILLNESSES OF CHILDHOOD

According to some authors acute illnesses of childhood such as measles, scarlet fever and chorea are etiologic factors. Fisher (1889) stated that during such an illness there is a transient paralysis of the dorsal flexors of the foot and that subsequently the child is weak and awkward for a few weeks. Then apparent recovery takes place and later, as the foot grows, the plantar fascia does not keep pace, and arching results. Shaffer reported having seen slight hemiplegia following scarlet fever and diphtheria and suggested that when this occurs the bones grow faster than the muscles and thus cause deformity. This theory does not appear sound since in many cases with paralysis or weakness of the dorsal flexors of the foot from a known cause, such as poliomyelitis, a clawfoot does not develop.

CONSTRICTION OF THE FEET DURING GROWTH

The wearing of shoes which do not fit or of tight shoes with high heels and the consequent habitual disuse of dorsal flexion are described as a cause of clawfoot. Boys usually wear well shaped shoes but exhibit the deformity as often as girls, and in girls clawfoot develops before improper shoes are worn. The occurrence of unilateral cases contradicts this theory.

A high longitudinal arch and limited dorsal flexion is occasionally seen in professional dancers, who use the muscles of the calf excessively. Some writers draw an analogy between clawfoot and the bound feet of Chinese women, but in the latter there is a calcaneocavus deformity without clawing of the toes.

MUSCULAR IMBALANCE

Intrinsic Muscular Imbalance.—Paralysis of the intrinsic muscles of the foot with active extrinsic muscles is the mechanism most frequently accepted as the cause. According to Duchenne the deformity occurs as follows: The normal action of the interossei is to flex the first phalanges of the toes and extend the last two. These therefore offer a resistance to the action of the long and short extensors, which alone overextend the first phalanges and flex the last two. If the action of the long and short extensors is unopposed by the interossei the toes are drawn back onto the metatarsal bones, the heads of which are depressed

and the bases raised, so that the arch is increased and a contraction of the plantar fascia follows.

There is substantial evidence against this theory. No definite paralysis or weakness of these muscles has been demonstrated by examination, by electrical stimulation or by dissection of a typical clawfoot. In many persons with clawfoot who have been personally examined there was sufficient control of the toes to allow the presence of active interossei and lumbricales to be demonstrated. In the presence of active interossei and lumbricales hammer toe is readily produced by the exaggerated action of the long toe extensors in their attempt to aid in dorsal flexion of a foot which has already lost its flexibility owing to a cavus or equinus deformity. It can be demonstrated on a cadaver that tension on the long toe extensor and flexor tendons at the same time produces hammer toe. The intrinsic muscles of the foot are well developed structures and constitute a moderate portion of the muscle mass of the foot; therefore marked atrophy should be detectable by inspection and palpation. In poliomyelitis the intrinsic muscles are less often paralyzed than the extrinsic.

Extrinsic Muscular Imbalance.—The disturbance of muscular balance necessary to produce clawfoot has been ascribed to each group of extrinsic muscles. Some observers suggest that the balance of power in the foot is triangular, the three forces being the dorsal flexors, the intrinsic muscles of the sole and the muscles of the calf. They state that any disturbance of balance between them allows a cavus deformity to develop. Hammer toes are thought to be secondary.

Weakness of the peroneus longus, allowing the tibial muscles to overact, is the explanation offered by Golding-Bird. He stated that this imbalance would take the tension off the plantar fascia, allow it to contract quickly and render the cavus permanent. On the other hand, according to Tubby (1896), exaggerated action of the peroneus longus is a causative factor, and weakness of the anterior tibial has been suggested by several authors. Weakness of the muscles of the calf was advanced as the cause of clawfoot by Barwell (1865) and more recently by Royle (1927). Altakoff (1931) published an article with illustrations of a model to demonstrate his theory that overactivity of the calf muscles causes clawfoot. He stated that after the limit of plantar flexion at the ankle joint is reached the calcaneus is pressed forward, pushing up the head of the talus and allowing the forefoot to be dragged down by the plantar fascia. Hammer toes are then produced by the overacting long toe extensors.

That muscular imbalance is important in the minds of many students of this condition is obvious from the aforementioned references and from the fact that much work is being done in an attempt to show the presence of very slight changes in the power of individual muscles.

This is necessary in order to uphold the theory of muscular imbalance, because by ordinary clinical means no weakness can be demonstrated in a typical clawfoot.

These theories of muscular imbalance are probably rendered untenable by the fact that many feet with definite weakness of muscles or groups of muscles have been observed for long periods without showing clawfoot. For instance, a valgus deformity with slight equinus and forefoot abduction usually follows paralysis of the anterior tibial muscle. A varus deformity without marked cavus follows paralysis of the peroneus longus muscle. Moderate equinus deformity follows paralysis of the long toe extensors. Weakness of the calf muscles, with strong posterior tibial and peroneus longus muscles, yields a deformity resembling clawfoot but lacks its stiffness and hammer toe deformity.

PARALYSIS IN THE FOOT FOLLOWING POLIOMYELITIS

Clawfoot associated with other residuals of poliomyelitis is frequent. Shaffer's observation that the deformity develops after the paralysis of the extremity has apparently entirely disappeared, or occurs in the opposite supposedly sound foot, has been confirmed repeatedly. He thought that the condition might be the result of imperfect recovery of power, leaving a slightly disturbed muscular imbalance. He could find no definite loss of power as measured with the faradic current. In discussing the occurrence of clawfoot in the absence of a history of poliomyelitis he said, "There is in none of my cases any history which leads me to think of the spinal cord; on the contrary, the clinical picture points to another motor tract, viz., that of the brain."

Weakness of the intrinsic muscles of the foot due to paralysis from mild unrecognized attacks of poliomyelitis is a favorite theory among orthopedic surgeons and has been discussed under intrinsic muscular imbalance.

Since the epidemic of 1931, 341 cases of poliomyelitis have been followed at the New York Orthopaedic Dispensary and Hospital. In approximately 40 of these the development of clawfoot was observed, occurring after a definite transient paralysis with complete recovery of power as determined by clinical examination. The latent period of its appearance varied from three to twenty-four months. Clawfoot occasionally developed in feet having definite paralysis at the time.

DISEASES OF THE CENTRAL NERVOUS SYSTEM

Deformities of the foot follow a great variety of diseases of the nervous system. Typical clawfoot is frequent in Friedreich's ataxia, interstitial hypertrophic neuritis of childhood, neuritic muscular atrophy (the peroneal types of Charcot-Marie-Tooth), spastic paralysis, poliomyelitis and tumor of the spinal cord. Kraus (1922) wrote on the

relation of clawfoot to diseases of the nervous system and listed many conditions in which he had observed an almost identical deformity.

HEREDITY

Clawfoot is common among the deformities associated with progressive familial diseases of the central nervous system. Friedreich's ataxia has been traced through several generations by Alpers and Waggoner (1929). Plowright (1928) described a family of eleven children, five of whom had cerebellar disease, and three of these had clawfeet. Clawfoot has been observed frequently with spina bifida and with congenital syphilis. The "idiopathic" type of the deformity is not thought to be inherited.

TRAUMA AND INFECTION

Peripheral nerve injury and cicatricial contracture produce deformity of the foot, at times with definite cavus, but a typical clawfoot rarely develops. Isolated cases have been reported following ischemic paralysis, cellulitis or abscess of the sole of the foot and plantar "rheumatism." Sometimes Friedreich's ataxia or another known cause of clawfoot is also present in cases in which a history of injury to the foot is given.

EVIDENCE POINTING TOWARD THE CENTRAL NERVOUS SYSTEM AS THE SITE OF THE CAUSATIVE LESION

From the foregoing discussion it will be noted that the known causes of clawfoot, with the possible exceptions of trauma and infection, are lesions of the central nervous system. In various neurologic conditions which frequently produce clawfoot extensive pathologic changes occur in the posterior and lateral columns of the spinal cord, especially in the spinocerebellar tracts and in Clarke's column. These areas are involved regularly in Friedreich's ataxia and often in neuritic muscular atrophy, congenital syphilis, poliomyelitis and interstitial hypertrophic neuritis of childhood (Wechsler 1927). Cerebellar disease has been described with clawfoot (Plowright 1928).

The frequent occurrence of clawfoot after poliomyelitis with no apparent paralysis of the foot suggests that the causative lesion is in the spinal cord and may be similar to that found in the neurologic disorders cited. A study of sections of the spinal cord after poliomyelitis shows that there is extensive damage in addition to destruction of the cells of the anterior horn. It has been reported that death of neurons occurs at the bases of the posterior horns and especially in the cells of Clarke's column (International Committee for the Study of Infantile Paralysis, 1932). There is a remarkable proliferation of connective tissue in the posterior and lateral columns and degeneration of nerve fibers in the

anterior and lateral columns of the white matter. Sections of the spinal cords of monkeys with poliomyelitis in the stage of repair reveal secondary degeneration in the anterolateral and cerebellar tracts and in the posterior columns.

The first report of a microscopic examination in a case of poliomyelitis was that of Cornil in 1863 while in Charcot's service. The patient had poliomyelitis at the age of 2 years and died of cancer forty-seven years later. Cornil found considerable atrophy of the anterolateral bundles of the cord. Nearly a decade later Charcot (1872) commented on the fact that both he and Cornil had completely overlooked the lesions in the motor cells.

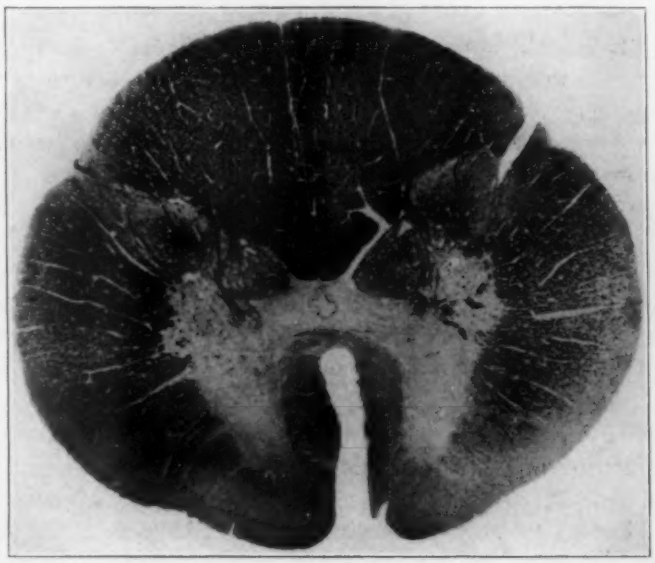

Fig. 1.—Section of the spinal cord of a child aged 1 year and 5 months after an attack of poliomyelitis. The section is stained for myelin by the del Rio Hortega method and shows loss of myelin in the anterior horns and also in the anterolateral columns of the white matter (reproduced from: International Committee for the Study of Infantile Paralysis: Poliomyelitis, 1932).

A rare ataxic type of poliomyelitis has been described with no involvement of the motor nerve cells. The anatomic basis for this condition is established by postmortem observation of involvement of the cerebellum, Clarke's column and the intervertebral ganglions. Howe (1919) stated:

> It would appear that the virus of anterior poliomyelitis does not have the peculiar affinity for the nerve elements of the cerebellum which it shows for the motor cells of the cord, and that the symptoms referable to the cerebellum are produced by interference with the function of its connecting nerve tracts and not by the destruction of its inherent nerve elements.

Further evidence of altered function of the spinal cord in poliomyelitis, in addition to the paralysis, is probably to be found in the frequent circulatory disturbance in the skin and in the occurrence of short metatarsal bones (Ferguson 1933). These phenomena are not directly related to the extent of the paralysis.

The function of the cerebellum is not definitely known; however, neurologists agree that it is the great synergizing organ of the central nervous system and that involvement of the spinocerebellar tracts produces a lack of coordination in muscular tone by interrupting the cerebellar reflex arcs. Patients with poliomyelitis and clawfoot rarely show evidence of ataxia, although numerous tests for it have been made. During observation of the development of clawfoot in children with poliomyelitis it was noted that a definite stiffness occurred with no real spasticity before the appearance of structural changes. In Friedreich's ataxia altered muscular tone and deformity occur before atrophy is demonstrable.

Loss of synergetic control of muscular tone is suggested as a possible explanation for the occurrence of clawfoot. The balance of power of muscles acting on the foot is thought to be disturbed so that deformity develops through their altered synergetic action in a way similar to the production of clawfoot in spastic paralysis of childhood or in Friedreich's ataxia. It is realized that in many cases there is no direct evidence of a lesion in the spinal cord and that further investigation will be necessary to establish this theory.

PROGNOSIS

Clawfoot of marked degree is disabling and distressingly painful. There is little definite knowledge concerning its rate of development, but it is known to vary markedly. Mills (1924) said that in many cases the deformity is not progressive and advocated conservative treatment. Jones and Lovett (1929) stated that ordinary paralytic clawfoot tends to reach a certain stage and then remain stationary. Observation of cases developing since the epidemic of poliomyelitis in 1931 corroborate these statements. The deformity was found to develop rapidly while the patients were in bed with the feet in plaster boots. It appeared often from two to six months after the acute attack. Progress in these cases was rapid for from two to three months and then became slow. After the primary cause has ceased to act growth of the foot apparently influences the progress of clawfoot by the secondary changes in the bones, muscles and ligaments, but 3 patients with moderate deformity have been observed for over four years during the adolescent period of growth with no increase in the deformity as determined by roentgenograms and clinical examination. On the other hand, in 6 the deformity definitely increased during the same period. They were treated by metatarsal bars and exercises.

When associated with diseases of the central nervous system in which nervous disturbances are continuous and progressive, clawfoot is known to increase steadily until late in adolescence.

The proper selection of measures to allow reestablishment of muscular tone and to correct deformity is necessary for lasting improvement. Relief can be assured in nearly every case by well planned treatment.

TREATMENT

The aim in each case should be to relieve symptoms, correct the deformity and prevent recurrence. The trend has been toward more radical procedures even in the milder cases, but every foot is an individual problem and must be treated accordingly. No rigid method can be stated. However, an outline of treatment based on the degree of deformity is suggested.

Fig. 2.—Structural cavus deformity of moderate degree. The site of resection advised is shown by the solid lines.

Slight Deformity.—In cases of flexible feet with moderate cavus which disappears on weight bearing special shoes with a low heel and a metatarsal bar should be worn; exercises to increase dorsal flexion and flexibility of the foot and stretching of the toes and muscles of the calf are recommended.

Moderate Deformity.—In feet with definite cavus, a loss of flexibility and hammer toes, lengthening of the calcaneus tendon, transplantation of the long toe extensor tendons to the cuneiform bones and arthrodesis of the interphalangeal joint of the first toe are advocated. For a markedly plantar-flexed first metatarsal, transplantation of the extensor hallucis longus tendon to the neck of the first metatarsal and lengthening of the peroneus longus tendon are recommended.

Marked Deformity.—In feet with stiff conspicuous cavus on weight bearing and marked hammer toe deformity an anterior tarsal resection,

in addition to the measures enumerated, is advised. Fasciotomy is rarely necessary.

Severe Deformity.—In extreme rigid cavus with varus of the heel an anterior tarsal resection is sufficient to correct the deformity in selected cases. If correction of more than 40 degrees is necessary, a subtalar triple arthrodesis is usually a better procedure. It is indicated also with marked calcaneal position of the heel and with lateral instability of the foot. To correct rigid hammer toes it is necessary to perform an arthrodesis of the proximal interphalangeal joints of the toes in addition to transplanting the long toe extensor tendons. At times it is necessary to release the contracted ligaments of the joint capsules.

The procedures suggested for a clawfoot of moderate degree are recommended for the more severe grades in addition to the correction

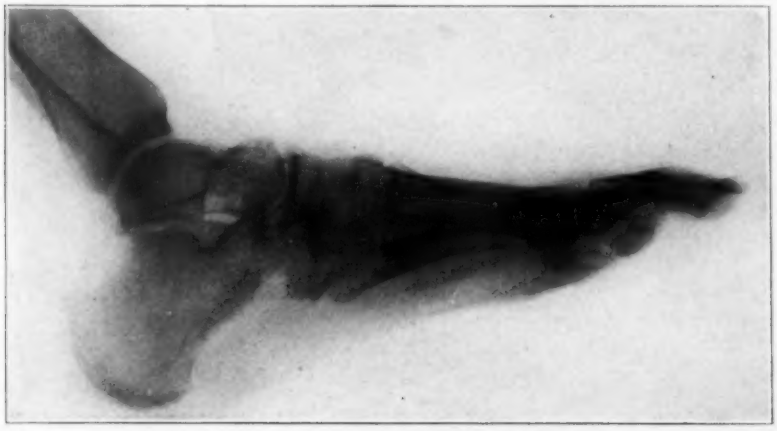

Fig. 3.—Same foot as that shown in figure 2. Anterior tarsal resection has been done with correction of the cavus deformity.

of bony deformity. Forceful wrenching, osteoclasis, etc., are condemned because they produce great trauma and are usually followed by early recurrence of deformity.

In some cases with no equinus deformity correction of the cavus condition by tarsal resection relaxes the long toe extensor tendons sufficiently to allow the toes to lie flat.

The treatment of clawfoot due to Friedreich's ataxia or other progressive diseases of the central nervous system should be the same, or perhaps more radical, because of its progressive and severe nature. The advisability of operating on these patients is questioned by some. The advice of several neurologists consulted is that the patients be kept as active as possible. For this reason it seems worth while to perform what operations are at hand to give these persons comfortable and stable feet.

STUDY OF ONE HUNDRED AND TWO FEET TREATED BY ANTERIOR TARSAL RESECTION

In order to determine the results in the treatment of clawfoot by anterior tarsal resection a study was made of the feet on which the operation to correct the cavus deformity was performed between March 14, 1927, and Oct. 21, 1931. Prior to this period resection of bone from the midtarsal region was the procedure used at the New York Orthopaedic Hospital.

For an anterior tarsal resection feet were selected in which the deformity was considered too great to respond to conservative measures or to operation on the soft tissues only. In cavus feet with

Fig. 4.—Structural cavus deformity with slight calcaneus position of the heel. This roentgenogram was taken with the patient standing.

varus deformity or lateral imbalance a subtalar triple arthrodesis was performed, as it was considered a more suitable procedure.

Surgical Procedure.—A tourniquet was used. A linear incision was made on the dorsum of the foot from ½ inch (1.27 cm.) below the center of the ankle joint to the base of the third metatarsal. The vessels were retracted medially. The navicular and cuneiform bones were exposed subperiosteally, and a wedge-shaped resection with the base dorsal was done, including the naviculocuneiform joints and continuing through the central portion of the cuboid. Sufficient bone was removed to allow complete correction of the cavus deformity. Adduction of the forefoot was corrected by widening the resection laterally. The plantar fascia rarely needed to be divided. A plaster boot was worn for six weeks, after which weight bearing was allowed either with or without plaster support, according to the roentgenographic evidence of union.

The anterior tarsal resection alone was done on 52 feet, and on 50 others additional operations were employed to correct hammer toe and equinus deformities.

The long toe extensor tendons were transplanted to the cuneiform bones in 28 of the feet by the method described by Hibbs in 1919. The tendon of the extensor hallucis longus muscle was transplanted into the neck of the first metatarsal in 3 feet. An arthrodesis of the interphalangeal joint of the great toe was always considered advisable when this tendon was transplanted either alone or with the other long toe extensor tendons. If this is not done hyperflexion of the interphalangeal joint is likely to occur and allow pressure areas to develop on the prominent knuckle. Usually the other toes do not require this. The calcaneus tendon was lengthened in 5 feet during the patient's period of hospitalization for the anterior tarsal resection. It was lengthened later in 16 as it was found to be a valuable procedure. The plantar fascia was seldom found tight enough to prevent correction of the cavus deformity by the resection. It was divided 9 times. The medial sesamoid bone of the great toe was later removed from three feet for persistent pain under the first metatarsal head. In 1 foot the

Fig. 5.—Same foot as that shown in figure 4. The structural cavus deformity has been corrected by an anterior tarsal resection. Notice the improved relationship of the calcaneus to the tibia. This roentgenogram was taken with the patient standing.

varus deformity of the heel increased, and a subtalar triple arthrodesis was necessary two years later.

There were 86 patients in this group, including 16 with bilateral deformities, making a total of 102 operations to be studied. Forty-one of the patients were males and 45 females. The diagnosis was clawfoot of unknown etiology in 29 feet, residual of poliomyelitis in 66, spastic paralysis in 5, and Friedreich's ataxia in 2. In some cases the diagnosis was uncertain. The average age at the time of operation was 13.9 years, the youngest patient being 7 years and the oldest 35. Sixty operations were done on the right foot and 42 on the left.

An attempt was made to evaluate the symptoms as reported preoperatively, but since the records were often found to be incomplete and inaccurate no special emphasis is placed on this part of the study. In the large group of patients with poliomyelitis the opposite lower extremity was often extensively paralyzed, and

the attention of both the examiner and the patient was focused on it. Some patients had had operations to correct deformities of the hip or knee which had no direct bearing on the clawfoot. Deformity was the most common symptom. However, 27 patients definitely complained of pain and 40 of easy fatigue. Tender callosities, corns and deformed toes were frequently mentioned. Many complained of stiffness, frequent stumbling and akwardness, and their parents mentioned the difficulty of finding shoes to fit the patients and spoke of the rapid wear of the shoes.

Definite structural cavus deformity was present in all the feet; it was severe in 43. Dorsal flexion was limited to 95 degrees or more in 72 feet. Varus position of the heel from slight to 15 degrees was noted in 33 feet. Ninety-nine of the feet were described as having a hammer toe deformity. Callosities and corns were distressing in many of them and were noted on examination in 54. The musculature was considered normal in 73 feet. Twenty-nine showed muscular weakness but no lateral instability. External rotation of the tibia was present in 1 case.

In estimating the results of the operation, function, symptoms and correction of deformity were carefully studied. The minimum follow-up period was two years. The results are grouped as follows: excellent, 28; good, 31; fair, 41, and poor, 2.

The results classified as excellent reveal no cavus deformity; the toes are flat in walking; the feet are flexible; there is no limp; there are no tender callosities or corns; dorsal flexion is not limited, and the function is apparently normal, with no ache or pain after strenuous exercise or athletics.

The results classified as good differ from the excellent results only in that slight hammer toe persists; nontender corns or callosities are present, or there is limited dorsal flexion.

The results classified as fair show one or more of the following conditions: slight stiffness or a nonelastic gait, limited dorsal flexion, residual cavus deformity or residual hammer toes. A few patients in this group complain of easy fatigue and of an ache after walking more than one-half mile.

The 2 feet classified as showing poor results are unimproved. One of these was unstable laterally, and a subtalar triple arthrodesis was necessary; the other is unstable laterally, and a subtalar triple arthrodesis is advised.

The follow-up examination revealed that in 27 feet the cavus was incompletely corrected. It was overcorrected in 5, producing flatfoot in 4 cases and a rockerfoot deformity in 1.

Dorsal flexion at the ankle joint was limited to from 95 to 105 degrees in 51 of the feet at the last examination.

Twenty of the 33 feet in which there was varus deformity before operation still retain some of it. Marked varus of the heel was considered a contraindication for an anterior tarsal resection. However, in feet with marked cavus and slight forefoot adduction with a depressed first metatarsal and slight varus it was expected that the latter would disappear when the cavus and forefoot deformities were corrected.

Residual hammer toe deformity was found in 35 feet. In some of these the toes had remained straight for from six to eighteen months before recurrence.

Callosities and corns were still present in 24 feet. Three patients said that the callosities were worse. In 4 feet they disappeared for from one to two years and then recurred.

The results of the operation in the 29 feet with definite muscular weakness are listed in table 1.

No definite relationship between the age of the patient and the result was noted. Stiffness was more frequently observed in the feet of the older patients but most of them remarked that there was improvement in their gait in addition to the relief from symptoms. A tendency of the deformity to recur was observed to be more frequent in the younger age groups.

In table 2 the results in the group of patients treated by anterior tarsal resection only are compared with results in those having additional procedures.

A study of the 28 feet with excellent results shows that correction of equinus deformity is often necessary. Six feet in this group did not show limitation of dorsal flexion before the operation. In 18 the calcaneus tendon was lengthened. It is interesting that 8 of these feet showed muscular weakness.

TABLE 1.—*Results of Operations for the Correction of Muscular Weakness*

Muscles	Number of Cases	Results			
		Excellent	Good	Fair	Poor
Normal	73	20	24	29	0
Weak	29	8	7	12	2
Anterior tibial absent	6	0	1	3	2
Anterior tibial weak	13	3	4	6	0
Long toe extensors and flexors weak	3	2	1	0	0
Peroneal weak	4	2	1	1	0
Calf weak	1	0	0	1	0
Flail feet	2	1	0	1	0

TABLE 2.—*Results of Operations in Patients Treated by Anterior Tarsal Resection Only and in Those Having Additional Procedures*

Muscles	Number of Cases	Results			
		Excellent	Good	Fair	Poor
Anterior tarsal resection only	52	10	12	29	1
With additional procedures	50	18	19	12	1

Seventy-four feet had residual deformity or symptoms and could not be classed as showing excellent results. All but 2 of these, however, were improved. As a result of the follow-up examination it is believed that 51 show equinus deformity which should be corrected and that 37 would be benefited by transplantation of the long toe extensor tendons. In 9 feet with a plantar-flexed first metatarsal transplantation of the extensor hallucis longus tendon to the neck of the first metatarsal would help. In 7 cases the result probably would have been better had a subtalar triple arthrodesis been done because of lateral imbalance in the foot. Five of the feet are too flat and 1 has a markedly relaxed ankle joint.

Observation of these feet leads to the conclusion that symptoms tend to recur if equinus deformity remains. Complete correction by lengthening of the calcaneus tendon is urged so that the foot, when slightly inverted and with the knee straight, can be easily dorsiflexed to 90 degrees. This is especially important when the long toe extensor tendons are transplanted, since it has been found that equinus deformity often progresses after this procedure alone. Persistence of callosities

under the metatarsal heads and recurrence of hammer toe deformity are usually attributable to limited dorsal flexion. Aching feet, stiffness and easy fatigue are apparently often due to the same cause.

In clawfoot of moderate degree better results were often obtained after lengthening of the calcaneus tendon and transplantation of the long toe extensor tendons than after correction of the cavus deformity alone by tarsal resection in the same type of clawfoot. This is thought to be due to the establishment of better balance of muscular tone through the temporary inactivity of the calf muscles induced by the lengthening of the tendon.

Roentgenographic Observations.—A study was made of the structural deformity as revealed by roentgenograms. It was found that in a typical clawfoot of marked degree deformity occurs throughout the whole foot and takes place both in the bones and in the joints. The angle between the long axes of the talus and calcaneus averages 46 degrees, which is 6 degrees more than the average angle in a normal foot. In most cases the neck and head of the talus are curved slightly plantarward. The navicular is often definitely wedge-shaped with the base dorsad. The cuneiforms are similarly wedged about as frequently. Slight dorsal bowing of the metatarsals is rare. The first metatarsal is often plantar-flexed at the first cuneiform-metatarsal joint. The degree of cavus deformity was measured on roentgenograms of the foot in the weight bearing position, using the angle between the long axes of the calcaneus and the first metatarsal. This angle averaged 115 degrees preoperatively and 140 degrees after the anterior tarsal resection. Bony union was obtained in all but 2 cases; in these there was a pseudarthrosis between the navicular and first cuneiform bones.

CONCLUSIONS AND SUMMARY

Clawfoot is a structural deformity involving the entire tarsus and metatarsus. Hammer toes and contracture of the plantar fascia are thought to be secondary.

Weakness of muscles is not the cause of typical clawfoot.

Evidence is presented suggesting that the etiologic factor is a lesion in the spinal cord which disturbs the synergetic control of muscular tone. Poliomyelitis may be one of the causes of such a lesion.

After an attack of poliomyelitis there is often a rapid development of clawfoot with subsequent slow progress. Many mild cases of deformity can be controlled by conservative measures.

The methods of treatment, which vary according to the degree of deformity, are outlined.

Correction of equinus deformity by lengthening of the calcaneus tendon is strongly advised.

Correction of the structural cavus by anterior tarsal resection is a good procedure. It must frequently be combined with lengthening of the calcaneus tendon and transplantation of the long toe extensor tendons to the cuneiform bones.

The results in 102 clawfeet treated by anterior tarsal resection, with a minimum follow-up period of two years, are as follows: excellent, 28; good, 31; fair, 41, and poor, 2.

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MASSIVE INTRAVENOUS INJECTIONS

AN EXPERIMENTAL STUDY

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The injection of blood and of various drugs intravenously is one of the oldest therapeutic procedures that is used in modern medicine.

HISTORICAL SKETCH

The most complete record of intravenous infusions in the preantiseptic era is found in Fortescue-Brickdale's [1] exhaustive study published thirty years ago. He stated that the earliest recorded transfusion was given to Pope Innocent VIII in 1492. The unfortunate outcome to the recipient and to the donors discredited the procedure, and more than a century elapsed before transfusions were again alluded to, this time by de Colle of Padua in 1628. This was a significant date as Harvey's "Exercitatio anatomica de motu cordis et sanguinis" appeared the same year, and the intravenous injection of drugs became a rational procedure. Probably the first experimental infusions were given in 1656 by Christopher Wren (then professor of astronomy at Oxford, but later to achieve fame as England's outstanding architect), who obtained narcosis by injecting a solution of opium into the veins of dogs. These experiments were repeated by Fracassatus of Pisa in 1658.

Gladstone's [2] recent translation of Johann Elsholtz's "Clysmatica nova" (Berlin, 1655) indicated that the injection of blood and of various medications intravenously was widely practiced at that time. He termed this method the "new clyster" and observed:

> If a tankard of wine is poured into a river, the wine together with the water flows into the sea; in just the same way, whatever liquid is injected into a vein must necessarily reach the heart together with the circulating blood.

Elsholtz in 1661 injected water, Spanish wine, opium and other drugs into the crural veins of dogs. Finding that these infusions gave results similar to those obtained when the drugs were taken by mouth, he injected aquae plantaginis, cardui benedicti and extract of cochleariae

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This study was aided by a grant from the Valentine Research Fund.

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1. Fortescue-Brickdale, J. M.: A Contribution to the History of the Intravenous Injection of Drugs, Guy's Hosp. Rep. **58**:15, 1904.

2. Gladstone, E.: Clysmatica Nova (1665) by Johann Sigismund Elsholtz, California & West. Med. **38**:432 (June); **39**:45 (July); 119 (Aug.); 190 (Sept.) 1933.

into the veins of three human subjects without ill effects. He reviewed the literature and cited experiments by Fracassatus of Pisa, Lower of Oxford, Dionysius of Paris and Mollerius of Denmark in which infusions and transfusions were given to animals and human beings. The blood of animals was frequently injected into human subjects, and cures were reported in cases of syphilis, epilepsy and intractable fevers after the injection of the blood of calves and of sheep. This form of treatment increased in popularity, and conflicting claims of priority were advanced by individual physicians and by groups of physicians. Elsholtz attempted to reconcile these differences of opinion in the closing passages of his book by stating:

> Let the Italians contend with the French about their priority, and the English with the Germans; perhaps they all are right since their ideas about the subject coincide . . . nevertheless, since this question has been aired seriously here and there, it does not seem to me that I am mistaken, or that I am unjust to anyone, if I believe that I first made in suitable quantity and adequate variety the experiments in simple infusion on which this whole discovery depends and that I then first combined these experiments properly, and certainly this is the hinge on which the whole affair turns.

Despite this auspicious beginning and the absence of any mention of unfavorable results, many unrecorded fatalities resulted from reactions and from sepsis. So hazardous was the practice that transfusions were forbidden in several European countries and intravenous therapy fell into disrepute.

After a lapse of about one hundred years, a revival of interest in intravenous injections commenced at the beginning of the nineteenth century, and from 1802 to 1827 a journal devoted entirely to transfusions and infusions was published in Copenhagen. In 1823 Hale of Boston described the injection of a therapeutic dose of castor oil into his own circulation with transient but disagreeable effects. Magendie in the same year reported temporary benefit in four cases of hydrophobia from intravenous injections of 600 cc. of warm water. Hayem in 1855 injected a 0.6 per cent solution of sodium chloride into the veins of patients with cholera. Haford in 1869 reported favorable results following the intravenous injection of solutions of ammonia in patients bitten by poisonous snakes. The frequent outbreaks of cholera during the latter half of the nineteenth century furnished the chief indication for intravenous infusions during the period when Pasteur and Lister's teachings received their first widespread clinical application.

The modern story of intravenous infusion dates from 1891, when Matas [3] reported seven recoveries in nineteen cases of severe shock and hemorrhage following the intravenous administration of from 250 to

3. Matas, R.: A Clinical Report on Intravenous Saline Infusion in the Wards of the New Orleans Charity Hospital from June 1888 to June 1891, New Orleans M. & S. J. **9**:1 and 81, 1891-1892.

1,500 cc. of isotonic salt solution. He stated that in all cases of circulatory failure intravenous infusion of saline solution results in temporary restoration and that this benefit is permanent in syncope due to simple and uncomplicated hemorrhage. Mayo Robson [4] in 1893 reported a case of severe shock followed by recovery after 2,500 cc. of physiologic solution of sodium chloride was given intravenously. Mummery,[5] in the Hunterian Lectures for 1905, stated that intravenously injected saline solution directly combats the fall in blood pressure by diminishing the disproportion between the quantity of circulating fluid and the capacity of the circulatory system, and also diminishes the viscosity of the blood incident to shock. He recommended the use of from 180 to 200 cc. an hour until the blood pressure remains at a safe level.

Because of the danger of overburdening the heart by single large intravenous infusions and the difficulty encountered in finding suitable veins in patients requiring repeated injections, Friedmann [6] in 1912 devised an apparatus, somewhat similar to that used in treatments by rectal drip, through which physiologic solution of sodium chloride could be given intravenously for long periods. A rubber tube connected to a funnel and containing a glass dropper, permitting the regulation of the flow, led to a glass cannula which was inserted into a superficial vein at the bend of the elbow. With this apparatus he was able to inject from 3 to 5 liters of physiologic solution of sodium chloride over a period of twenty-four hours. The amount of fluid needed and the general condition of the patient determined the rapidity with which the fluid was given. Friedmann advised this method chiefly in cases of dehydration, such as cholera, diarrhea, ileus, carcinoma of the stomach, infectious diseases associated with collapse, peritonitis and sepsis. His conclusions, based on twenty cases in which the patient was treated by this method, were that the heart is not overburdened and sudden rises in the blood pressure are avoided, normal kidneys are stimulated to increased activity, the method is relatively free from discomfort, and the treatment may be continued until the condition of the patient improves sufficiently to warrant its discontinuance.

In 1924 Matas [7] reported a series of cases in which a 5 per cent dextrose solution in distilled water was given continuously through a

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4. Robson, M.: Severe Shock Treated by Transfusion or Infusion of Normal Saline Solution, Brit. M. J. **1**:697, 1893.

5. Mummery, J. P. L.: The Physiology and Treatment of Surgical Shock and Collapse, Lancet **1**:696 (March 18); 776 (March 25); 846 (April 1) 1905.

6. Friedmann, M.: Ueber intravenöse Dauerinfusion, München. med. Wchnschr. **60**:1022, 1913.

7. Matas, R.: Continued Intravenous "Drip," with Remarks on the Value of Continued Gastric Drainage and Irrigation by Nasal Intubation with a Gastro-Duodenal Tube (Jutte) in Surgical Practice, Ann. Surg. **79**:643 (May) 1924.

Murphy drip apparatus and a cannula tied in a vein. Dextrose, which had been used previously as a substitute for salt in subcutaneous infusions, was adopted because of its nutritive and stimulating properties and because of the danger of the retention of sodium chloride in prolonged administration. Matas felt that intestinal obstruction, septic peritonitis, disease of the biliary tract with hepatic insufficiency, advanced pyloric obstruction and surgical lesions of the kidney with threatened anuria are especial indications for the intravenous administration of dextrose. He first used this method in 1911 when the usual methods for the administration of fluid had failed. So impressed was he by the ease of administration and the marked benefit obtained by this method that he recommended broadening its scope to include the treatment of patients who probably would rally under the more commonplace measures.

Palmedo [8] in 1928 reported one hundred and fifty cases in which the patient was treated with continuous intravenous infusion. He regarded this method as an excellent emergency treatment in cases of shock and of hemorrhage and recommended its use in cases of peritonitis, of dehydrated conditions and of ruptured ectopic pregnancy, and as a preoperative and postoperative measure in cases of prolonged operation on the gastro-intestinal tract. He advocated continuous intravenous infusion of physiologic solution of sodium chloride whenever he would previously have resorted to subcutaneous infusions. Palmedo warned against overburdening the circulatory system with fluids because of possible cardiac damage and considered lesions of the kidney, high blood pressure, bronchitis and pneumonia as contraindications.

Warthen [9] reported a case of intestinal obstruction in 1930, following gastro-enterostomy and two subsequent operations with release of adhesions and entero-enterostomy in which 54,000 cc. of 5 per cent dextrose in physiologic solution of sodium chloride was administered over a period of eighteen days. This solution contained 2,700 Gm. of dextrose, or 10,800 calories, and was the only fluid or nutriment taken during this time. Autopsy revealed the presence of dense adhesions with multiple complete obstructions. There was no evidence of circulatory damage from this prolonged intravenous therapy. Intestinal obstruction, generalized peritonitis and toxemia following extensive burns were thought to be especial indications for its use. This method was invaluable for dehydrated patients when the usual oral, subcutaneous and anal routes of administration were for any reason inadequate to supply the physiologic needs. The author recommended the

8. Palmedo: Erfahrungen mit der intravenösen Dauertropfinfusion nach Friedemann, Arch. f. klin. Chir. **153**:734, 1928.

9. Warthen, H. J.: Continued Intravenous Dextrose, Internat. S. Digest **10**:3 (July) 1930.

injection of from 125 to 200 cc. of 5 per cent dextrose in physiologic solution of sodium chloride per hour for adults, with the additional administration of hypertonic salt solution in cases of intestinal obstruction to supplement the chlorides in the blood. Dextrose in distilled water was given to patients with nephritis or to those who showed evidence of retention of salt.

Hendon [10] employed the term "venoclysis" to designate this form of therapy and recommended the use of 10 per cent dextrose in isotonic salt solution administered at the rate of 200 cc. an hour. He found this solution of especial value for the vomiting of pregnancy and reported a surprising increase in the red blood cell counts of patients with pernicious anemia after intravenous infusions.

Various combinations of chlorides have been used as solvents to approximate closely the constituents of normal blood serum. Horsley and Horsley [11] in 1931 recommended the use of 5 per cent dextrose in Ringer's solution (0.7 per cent sodium chloride, 0.03 per cent potassium chloride, and 0.025 per cent calcium chloride in distilled water). They found this solution to be of great value when given intravenously during and after extensive operations on the gastro-intestinal tract and in cases of intestinal obstruction. It was also of value in duodenal fistula when large amounts of fluid were lost, in the vomiting of pregnancy, in diarrhea, in dysentery, in toxic goiter and in hyperthyroidism.

Melzner [12] in 1931 recommended a more widespread use of intravenous infusions and regarded physiologic solution of sodium chloride as the solution of choice. He advised that intravenous injections of fluids be made with caution in the presence of myocardial weakness and disease of the kidney.

Hyman and Hirshfeld,[13] in 1933, in addition to the usual indications for intravenous fluids, recommended from 5 per cent to 10 per cent dextrose in physiologic solution of sodium chloride as a vehicle for massive intravenous doses of specific antiserums, such as antipneumococcus serum or tetanus antitoxin, in metabolic and toxic conditions, for instance, dehydration in infants, and mercurial poisoning.

Titus and Lightbody [14] stated that overdosage and underdosage have been common faults owing to the fact that the actual therapeutic intra-

10. Hendon, G. A.: Venoclysis, J. A. M. A. **95**:1175 (Oct. 18) 1930.

11. Horsley, J. S., and Horsley, G. W.: Continuous Intravenous Injection of Dextrose in Ringer's Solution, Arch Surg. **22**:86 (Jan.) 1931.

12. Melzner, E.: Intravenöse Dauertropfinfusion, München. med. Wchnschr. **78**:1983 (Nov. 20); 2039 (Nov. 27) 1931.

13. Hyman, H. T., and Hirshfeld, S.: Therapeutics of Intravenous Drip, J. A. M. A. **100**:305 (Feb. 4) 1933.

14. Titus, P., and Lightbody, H. D.: Report of Investigations to Determine the Therapeutic Dose of Dextrose Administered Intravenously, Am. J. Obst. & Gynec. **18**:208 (Aug.) 1929.

venous dose of dextrose has not been known. They recommended a 25 per cent dextrose solution and suggested that 25 Gm. of dextrose should be given in not less than thirty or thirty-five minutes to an average adult, and limited the therapeutic intravenous dose to 75 Gm. injected over a period of from ninety to one hundred minutes. They felt that less than this amount will not give the maximum therapeutic effect and more than this is likely to produce a reaction from overstimulation of the insulin-producing activity of the pancreas. Because of this they recommended single intravenous doses of dextrose repeated from one to three times daily in preference to prolonged injections, and suggested the possibility that "reactions" during injections of dextrose may be due to hypoglycemia from prolonged overdosage of dextrose causing an overstimulation of the pancreas.

Fatalities following intravenous infusions have occurred. Clark [15] reported three cases in which death followed the injection of small amounts of 10 per cent dextrose and physiologic solution of sodium chloride. These fatal cases were characterized by chills, precordial pain, cyanosis and death in from two to nine hours after the injection. Clark attributed these fatalities to acute cardiac dilatation caused by the overburdening of a supposedly normal heart which had been previously weakened by nervous, operative or toxic trauma.

These references indicate the wide range of conditions in which intravenous infusions may be employed, the gradual increase in the amount of solution that is infused and the present diversity of opinion as to the best solution for intravenous use.

Despite the frequency with which large amounts of dextrose or of salt solution of various concentrations are injected intravenously, little is known about the changes in the blood caused by the addition of these solutions or about the total amount of fluid which can be given by this route without embarrassing the circulatory system. This has been due in part to the fact that the amount of the solution injected has been gradually increased over a period of several decades. Attempts to study the changes in the blood chemistry produced by large intravenous infusions have also been handicapped because the treatment has been used frequently as an emergency measure for acutely ill patients and because of the desire to avoid unnecessary venipunctures in patients requiring subsequent intravenous treatments.

In order to avoid these unfavorable circumstances, at the suggestion of Dr. Dean Lewis, a study of the changes in the blood chemistry following infusions has been made in a series of experimental animals, and varying amounts of solution have been injected to determine the

15. Clark, J. H.: Acute Cardiac Dilatation: An Ever Present Danger in Intravenous Injections, J. A. M. A. **89**:21 (July 2) 1927.

quantity which can be infused without causing death or untoward symptoms.

It has long been known that animals can tolerate large amounts of intravenous fluids. Cohnheim and Lichtheim [16] in 1877 injected a 0.6 per cent solution of sodium chloride in dogs and in rabbits in a study of experimental edema. The fluid was injected by gravity pressure into the jugular vein until the animal died. They found that a rabbit could absorb 46 per cent of its body weight within two hours, and one dog with an opened abdomen received fluid which equaled 92 per cent of its weight before it died. The rabbits as a rule died earlier than the dogs, because of the frequent occurrence of pulmonary edema. The dogs rarely showed this complication and usually died of cardiac weakness or in convulsions. There was less proportional effect on the concentration of the blood with large intravenous infusions than with smaller ones. A moderate increase in the arterial pressure was noted early in the experiments, followed later by a fall in the pressure as the infusions were continued. This may indicate that the total amount of fluid given in these experiments was not a true index of the lethal dose, as a considerable amount of fluid may have been forced into a failing circulation after the animal was obviously moribund. The infusions were accompanied by a steady rise in the venous pressure which increased in proportion to the amount of fluid injected.

Two articles of interest on this subject have recently appeared. Blalock, Beard and Thuss in 1932 [17] injected various fluids into the veins of dogs at the rate of 10 cc. per kilogram of body weight per hour. The average duration of the infusion was four hours. They found that 75 per cent of the fluid passed into the serous cavities and tissue spaces. There was no marked alteration in the blood pressure as a result of the infusions.

Miller and Poindexter in 1932 [18] injected isotonic sodium chloride solution intravenously and subcutaneously in dogs in an attempt to find a method of determining a deficit or excess of fluid in the body tissues. Although an increase in the volume of circulating blood could not be demonstrated by the vital dye method, the average red cell count and hemoglobin content were decreased more than 20 per cent by the intra-

16. Cohnheim, J., and Lichtheim, L.: Ueber Hydrämie und hydrämisches Oedem, Virchows Arch. f. path. Anat. **69**:106, 1877.

17. Blalock, A.; Beard, J. W., and Thuss, C.: Intravenous Injections: A Study of the Effects on the Composition of the Blood of the Injection of Various Fluids into Dogs with Normal and Low Blood Pressures, J. Clin. Investigation **11**:267 (March) 1932.

18. Miller, J. R., and Poindexter, C. A.: The Effects Observed Following the Intravenous and Subcutaneous Administration of Fluid; An Experimental Study on Dogs, J. Lab. & Clin. Med. **18**:287 (Dec.) 1932.

venous infusions. The total proteins in the blood were decreased, the reduction varying from 20 to 52 per cent with the various injections. The authors were unable to find any index which might serve as a warning against overhydration of tissues, but they stated that the hematocrit is the simplest test for determining the dilution of the blood following the postoperative administration of fluids.

EXPERIMENTS

Twenty-one dogs received forty intravenous infusions. Ten infusions were given of each of the four most frequently used solutions, namely 0.7 per cent sodium chloride, 5 per cent dextrose, hypertonic sodium chloride (1.5 per cent and 2 per cent) and 10 per cent dextrose. Twenty-eight infusions were given to ten dogs in the surgical clinic of the University of Freiburg.[19] Owing to the difficulty encountered in obtaining the larger experimental animals in Germany, it was necessary to give several infusions to the same dog. The largest number of intravenous infusions was given to dog 6. This dog received seven injections during a period of three months. Sufficient time was permitted to elapse between each two infusions to allow the dog to recover from the effects of the last injection. Determinations of the blood pressure could not be made in this first series of twenty-eight experiments as the procedure necessitated the ligation of the femoral artery with circulatory changes in the involved extremity. Owing to the difficulty of restraining unanesthetized animals for long periods of time, single massive infusions were given in the space of a few minutes rather than prolonged continuous infusions. Healthy dogs were used in these experiments, but no attempt was made to obtain young animals.

The experiments were performed in the following manner: The weight of the dog was recorded and a preoperative dose of morphine (10 to 20 mg. per kilogram of body weight) was given. The majority of the experiments were performed under local anesthesia in order to approximate normal conditions as nearly as possible. Five animals received ether or diallyl-barbituric acid. An incision was made so as to expose the femoral vein. Fifteen cubic centimeters of blood was withdrawn for chemical analysis, and a cannula or a needle was inserted in the vein through which the solution was infused under gravity pressure. The temperature of the infused solutions was kept at 100 F. At the conclusion of the experiment another sample of blood was withdrawn for chemical determinations.

In the first few infusions only 1,000 cc. of solution was injected over a period of thirty or forty minutes, but this amount was so well tolerated that the infusions were gradually increased until on one occasion 2,600 cc. of fluid was given in twenty-six minutes.

Chemical determinations[20] were made of the blood sugar, nonprotein nitrogen and chlorides, expressed in milligrams per hundred cubic centimeters of blood, before and after each infusion. The resistance of the red blood cells to hemolysis by various hypotonic solutions of sodium chloride was also determined in order

19. Warthen, H. J.: Ueber intravenöse Infusion in grossen Mengen; eine experimentelle Studie, Beitr. z. klin. Chir. **159**:51 (Jan.) 1934.

20. The nonprotein nitrogen was determined by the Folin and Wu method. The blood sugar was determined by a modification of the Folin and Wu method. The blood chlorides were determined by the Whitehorn method. The blood chlorides are expressed as sodium chloride throughout this paper.

to note any change that occurred following large infusions. The pulse rate was observed, symptoms were noted and the condition of the dog at the conclusion of the experiment was recorded. Determinations of blood pressure were made during twelve infusions. In order to have a standard for comparison, the amount of fluid infused into each dog was calculated in cubic centimeters per kilogram of body weight.

In each of tables 1 to 4 the first seven experiments recorded were performed in Germany and the last three experiments were performed in this country. In order to facilitate a comparison of these two subgroups the average values are given separately in each table. At the bottom of each column a final average is given which includes all of the experiments in the table. Unless otherwise specified, all references to average values refer to the final average.

Series 1 (*Infusion of 0.7 Per Cent Sodium Chloride Solution*).—Six dogs received ten infusions of 0.7 per cent sodium chloride solution in amounts varying from 65 to 175 cc. per kilogram of body weight. The average amount injected was 106 cc. per kilogram of body weight. The average duration of the infusions was thirty minutes.

The average nonprotein nitrogen content of the blood before the infusions was 23.2 mg. per hundred cubic centimeters; after the infusions it was 18.9 mg., showing a decrease of 4.3 mg. The average blood sugar value before the infusion was 128 mg. per hundred cubic centimeters; after the infusions it was 147 mg., showing an increase of 19 mg. The average blood chloride content rose from 633 mg. per hundred cubic centimeters to 709 mg., showing an increase of 76 mg. The resistance test showed a very slight increase in the fragility of the red blood cells following the infusions. Hemolysis began with a concentration of sodium chloride of 0.42 per cent and was complete with a concentration of 0.32 per cent before the infusions, and began with a 0.43 per cent concentration and was complete with a 0.33 per cent concentration after the infusions.

Two dogs in this series voided before the end of the infusion. The pulse rate, which was usually slow at the beginning of the injections as a result of the morphine, increased during the injections, gradually returning to normal after the conclusion of the infusions. No reactions occurred, and the condition of all of the dogs was satisfactory at the conclusion of the experiments. No deaths resulted from the infusions.

Series 2 (*Infusion of 5 Per Cent Dextrose Solution*).—Eight dogs received ten infusions of 5 per cent dextrose solution in amounts varying from 71 to 210 cc. per kilogram of body weight. The average amount injected was 134 cc. per kilogram of body weight. The average duration of the infusions was twenty-four minutes.

The average nonprotein nitrogen content of the blood before the infusions was 29.7 mg. per hundred cubic centimeters; after the infusions it was 22.5 mg., showing a reduction of 7.2 mg. The average blood sugar value before the infusions was 124 mg. per hundred cubic centimeters; after the infusions it was 454 mg., showing an increase of 330 mg. The average blood chloride content diminished from 643 mg. per hundred cubic centimeters to 612 mg., showing a decrease of 31 mg. The resistance test showed a slight increase in the resistance of the red blood cells to hemolysis following the infusions. Hemolysis began with a concentration of sodium chloride of 0.45 per cent and was complete with a concentration of 0.33 per cent before the infusions and began with a 0.44 per cent concentration and was complete with a 0.32 per cent concentration after the infusions.

TABLE 1.—*Infusion of 0.7 Per Cent Sodium Chloride Solution*

Experiment No.	Dog No.	Anesthetic*	Weight, Kg.	Duration, Minutes	Total Amount Given, Cc.	Cc. per Kg. of Body Weight	Nonprotein Nitrogen, Mg. per 100 Cc.		Blood Sugar, Mg. per 100 Cc.		Blood Chlorides, Mg. per 100 Cc.		Fragility of Red Blood Cells†		Comment
							Before	After	Before	After	Before	After	Before	After	
1	3	P	12.5	22	1,000	80	14.0	19.6	103	122	...	...	0.42 0.32	0.42-0.32	Voided once
2	5	P	23.0	40	1,500	65	28.0	16.4	104	92	742	859	0.38-0.30	0.40-0.30	No reaction
3	3	P	12.3	30	1,500	122	17.5	18.2	148	136	590	637	0.44-0.30	0.44-0.30	No reaction
4	6	P	17.0	25	1,750	103	15.1	12.5	151	192	661	754	0.44-0.34	0.40-0.34	No reaction
5	5	P	22.5	30	2,000	88	10.5	16.5	137	141	497	544	0.42-0.32	0.42-0.34	Voided once
6	5	P	20.0	30	2,250	112	33.9	18.5	92	124	819	971	0.40-0.30	0.40-0.32	Slight dyspnea
7	6	P	17.0	40	2,500	147	18.5	6.0	132	117	748	865	0.44-0.32	0.48-0.32	No reaction
Average for first seven dogs			17.7	31	1,785	102	19.7	15.4	124	132	676	771	0.42-0.31	0.43-0.33	
8	11	P	11.3	25	1,500	133	33.8	26.0	158	174	476	570	0.36	0.38	No reaction
9	12	P	15.9	30	950	60	27.0	24.0	146	232	520	612	0.36	0.34	No reaction
10	15	E	14.8	26	2,600	175	34.0	32.0	115	139	544	568	....	....	No reaction
Average for last three dogs			14.0	27	1,683	123	31.6	27.0	140	182	513	583	0.36	0.36	
Average for entire group			16.6	30	1,755	106	23.2	18.9	128	147	633	709	0.42-0.32	0.43-0.33	

* P represents 2 per cent procaine hydrochloride; E, ether.

† The figures represent the concentrations of sodium chloride with which hemolysis began and was complete.

TABLE 2.—*Infusion of 5 Per Cent Dextrose Solution*

Experiment No.	Dog No.	Anesthetic*	Weight, Kg.	Duration, Minutes	Total Amount Given, Cc.	Cc. per Kg. of Body Weight	Nonprotein Nitrogen, Mg. per 100 Cc.		Blood Sugar, Mg. per 100 Cc.		Blood Chlorides, Mg. per 100 Cc.		Fragility of Red Blood Cells†		Comment
							Before	After	Before	After	Before	After	Before	After	
11	2	P	8.7	40	1,000	115	....	....	98	415	...	...	0.46-0.28	0.36-0.26	Voided twice
12	3	P	10.0	30	1,000	100	28.7	11.2	113	561	623	669	0.44-0.34	0.43-0.30	Voided twice
13	4	P	14.0	20	1,000	71	15.8	5.2	...	...	695	715	0.47-0.39	0.55-0.35	No reaction
14	2	P	8.0	25	1,050	131	12.6	5.9	112	406	1,088	754	0.42-0.34	0.40-0.34	No reaction
15	2	P	9.2	25	1,500	163	25.2	14.0	84	184	561	508	0.42-0.28	0.38-0.24	Insulin, 60 units, voided twice
16	7	P	9.5	17	2,000	210	42.0	17.5	170	651	877	994	0.44-0.32	0.46-0.34	Voided once
17	6	P	15.0	24	2,400	160	27.3	18.6	134	551	649	678	0.42-0.32	0.42-0.32	No reaction
Average for first seven dogs			10.6	26	1,421	136	25.3	12.1	119	428	734	720	0.44-0.32	0.43-0.31	
18	16	E	15.2	38	2,000	132	36.4	44.0	105	480	502	332	.....	.....	No reaction
19	17	D	9.4	8	1,200	128	45.0	48.0	102	414	544	342	.....	.....	No reaction‡
20	21	P	17.0	13	2,200	129	34.0	38.0	200	426	536	404	0.50-0.34	0.50-0.36	Insulin, 50 units; voided once
Average for last three dogs			13.8	19	1,800	130	38.5	43.3	136	440	516	359	0.50-0.34	0.50-0.36	
Average for entire group			11.6	24	1,535	134	29.7	22.5	124	454	643	612	0.45-0.33	0.44-0.32	

* P represents 2 per cent procaine hydrochloride; E, ether; D, diallyl-barbituric acid.

† The figures represent the concentrations of sodium chloride with which hemolysis began and was complete.

‡ See text for continuation of infusion in experiment 19.

Five dogs in this series voided before the end of the infusion. One dog vomited during the infusion, probably a result of the preoperative injection of morphine. There was a marked acceleration of the pulse rate during the infusions. No reactions occurred, and the condition of all of the dogs was satisfactory at the conclusion of the experiments. No deaths resulted from the infusions. (See page 217 for a report of the continuation of infusion in experiment 19.)

Series 3 (Infusion of 1.5 Per Cent and 2 Per Cent Sodium Chloride Solution).—Seven dogs received eight infusions of a 2 per cent sodium chloride solution and two dogs received a 1.5 per cent solution. The results will be considered together. The smallest amount of solution infused was 60 cc. per kilogram of body weight, the largest was 182 cc. and the average was 112 cc. The average duration of the infusions was twenty-three minutes.

The average nonprotein nitrogen content of the blood before the infusions was 23 mg. per hundred cubic centimeters; after the infusions it was 22.8 mg., showing a decrease of 0.2 mg. The average blood sugar value before the infusions was 161 mg. per hundred cubic centimeters; after the infusions it was 138 mg., showing a decrease of 23 mg. The average blood chloride content rose from 575 mg. per hundred cubic centimeters to 731 mg., showing an increase of 156 mg. The resistance test showed practically no change as a result of the infusions; hemolysis began with a concentration of sodium chloride of 0.44 per cent and was complete with a concentration of 0.34 per cent before the infusions and began with a 0.44 per cent concentration and was complete with a 0.33 per cent concentration after the infusions.

No dog in this series voided before the end of the infusions. The increase in the pulse rate during the infusions was not so marked as was noted during the injections of the other solutions. The dogs in this series showed no reaction to the infusions aside from marked borborygmus during the injection of the solution. The condition of all of the dogs was satisfactory at the conclusion of the experiments, and no deaths resulted from the infusions.

Series 4 (Infusion of 10 Per Cent Dextrose Solution).—Nine dogs received ten infusions of 10 per cent dextrose solution in amounts varying from 57 to 189 cc. per kilogram of body weight. The average amount injected was 118 cc. per kilogram of body weight. The average duration of the infusions was twenty minutes.

The average nonprotein nitrogen content of the blood before the infusions was 25.7 mg. per hundred cubic centimeters; following the infusions it was 25.4 mg., showing a reduction of 0.3 mg. The average blood sugar value before the infusions was 158 mg. per hundred cubic centimeters; after the infusions it was 1,018 mg., showing an increase of 860 mg. This marked increase was due chiefly to two large infusions in which the blood sugar value rose to 1,670 and 2,500 mg., respectively. The average blood chloride content diminished from 564 mg. per hundred cubic centimeters to 487 mg., showing a decrease of 77 mg. The resistance test showed a definitely increased resistance to hemolysis following the infusions. Hemolysis began with a concentration of sodium chloride of 0.45 per cent and was complete with a concentration of 0.32 per cent before the infusions and began with a 0.42 per cent concentration and was complete with a 0.29 per cent concentration after the infusions. Insulin in doses varying from 40 to 200 units was given in nine of the ten experiments.

One dog in this series voided before the end of the infusion. The pulse rate increased markedly during the infusions in the majority of the cases, but gradually returned to normal following the injections. Two dogs made convulsive movements during the infusions, and three dogs died within twelve hours as a result of the infusions. (See page 218 for a description of the deaths.)

TABLE 3.—*Infusion of 1.5 Per Cent and 2 Per Cent Sodium Chloride* *

Experiment No.	Dog No.	Anesthetic†	Weight, Kg.	Duration, Minutes	Total Amount Given, Cc.	Cc. per Kg. of Body Weight	Nonprotein Nitrogen, Mg. per 100 Cc.		Blood Sugar, Mg. per 100 Cc.		Blood Chlorides, Mg. per 100 Cc.		Fragility of Red Blood Cells‡		Comment
							Before	After	Before	After	Before	After	Before	After	
21	9	P	6.8	18	1,000	147	17.2	13.3	172	162	614	678	0.42-0.34	0.42-0.34	No reaction
22	1	P	10.3	20	1,100	107	21.0	21.0	204	213	561	637	0.44-0.32	0.44-0.30	Borborygmus
23	8	P	24.0	22	1,500	63	27.6	34.8	103	67	561	661	0.42-0.34	0.42-0.34	Borborygmus
24	6	P	17.0	18	2,000	118	30.1	22.4	150	114	889	968	0.44-0.34	0.44-0.32	Borborygmus
25	6	P	15.4	18	2,000	129	16.8	31.9	142	63	529	643	0.40-0.34	0.42-0.32	Borborygmus
26	8	P	25.0	22	2,000	80	22.1	14.0	138	174	491	661	0.43-0.34	0.40-0.34	Borbarygmus
27	8	P	22.0	15	2,000	91	17.5	21.9	121	117	473	579	0.46-0.32	0.46-0.32	No reaction
Average for first seven dogs			17.2	19	1,657	105	21.8	22.6	150	130	588	692	0.43-0.33	0.43-0.33	
28	13	P	13.8	29	2,000	145	26.0	21.0	200	160	616	918	0.38	0.36	No reaction
29	14	P	11.0	36	2,000	182	29.4	28.0	160	125	454	848	0.38	0.38	No reaction
30	12	P	15.0	32	900	60	23.0	20.0	200	192	568	686	0.50-0.32	0.50-0.30	No reaction
Average for last three dogs			13.3	32	1,633	129	26.1	23.0	187	159	546	817	0.50-0.36	0.50-0.35	
Average for entire group			16.0	23	1,650	112	23.0	22.8	161	138	575	731	0.44-0.34	0.44-0.33	

* The 1.5 per cent concentration was used in experiments 23 and 24.

† P represents 2 per cent procaine hydrochloride.

‡ The figures represent the concentrations of sodium chloride with which hemolysis began and was complete.

TABLE 4.—*Infusion of 10 Per Cent Dextrose Solution*

Experiment No.	Dog No.	Anesthetic*	Weight, Kg.	Duration, Minutes	Total Amount Given, Cc.	Cc. per Kg. of Body Weight	Nonprotein Nitrogen, Mg. per 100 Cc.		Blood Sugar, Mg. per 100 Cc.		Blood Chlorides, Mg. per 100 Cc.		Fragility of Red Blood Cells†		Comment
							Before	After	Before	After	Before	After	Before	After	
31	9	P	6.7	16	1,000	149	17.9	16.1	194	2,500	614	356	0.38-0.30	0.36-0.24	No reaction; insulin, 40 units
32	6	P	17.0	45	1,300	76	24.5	17.5	127	804	772	625	0.48-0.36	0.46-0.36	Voided once; insulin, 60 units
33	1	P	10.2	20	1,500	148	15.4	6.3	251	936	573	380	0.40-0.28	0.38-0.26	No reaction; insulin, 100 units
34	6	P	17.5	20	1,500	86	23.8	21.2	124	933	643	310	0.44-0.34	0.42-0.32	No reaction; insulin, 45 units
35	8	P	26.5	15	1,500	57	32.6	30.1	98	941	690	807	0.44-0.32	0.44-0.34	No reaction; insulin, 50 units
36	7	P	9.5	15	1,800	189	26.6	24.9	170	1,670	631	1,134	0.42-0.32	0.36-0.22	Died 2 hours later‡
37	10	P	15.5	25	2,000	129	20.3	14.7	110	1,134	298	193	0.48-0.38	0.44-0.32	No reaction; insulin, 100 units
Average for first seven dogs			14.7	22	1,514	119	23.0	18.7	153	1,274	603	544	0.43-0.33	0.41-0.29	
38	19	P	13.9	20	2,000	144	35.0	44.0	109	346	426	380	.....	.....	No reaction; insulin, 200 units
39	20	E	15.0	13	2,400	160	32.8	38.4	240	474	556	366	0.50-0.32	0.46	Died in 12 hours;‡ insulin, 200 units
40	22	E	14.6	12	2,000	137	28.0	41.2	159	436	434	322	0.50-0.28	0.50-0.28	Died in 12 hours;‡ insulin, 150 units
Average for last three dogs			14.5	15	2,133	147	31.9	41.2	169	419	472	356	0.50-0.30	0.48-0.28	
Average for entire group			14.6	20	1,700	118	25.7	25.4	158	1,018	564	487	0.45-0.32	0.42-0.29	

* P represents 2 per cent procaine hydrochloride; E, ether.

† The figures represent the concentrations of sodium chloride with which hemolysis began and was complete.

‡ See text for analysis of deaths.

COMPARISON OF THE SODIUM CHLORIDE VALUES OF THE WHOLE BLOOD AND PLASMA [21]

The sodium chloride content of the whole blood was determined in thirty-eight of the forty experiments and the results of these determinations are given in tables 1 to 4. The sodium chloride content of the plasma was also obtained in eleven of these experiments. A comparison of the sodium chloride values is given in table 5.

TABLE 5.—*A Comparison of the Sodium Chloride Values of the Whole Blood and Plasma*

Experiment No.	Solution Infused	Amount Infused per Kg. of Body Weight, Cc.	Sodium Chloride, Mg. per 100 Cc.			
			Before		After	
			Whole Blood	Plasma	Whole Blood	Plasma
8	0.7 per cent sodium chloride...	133	476	572	570	606
10	0.7 per cent sodium chloride...	176	544	617	568	643
18	5 per cent dextrose.....	132	502	550	332	342
19	5 per cent dextrose.....	128	544	624	450	422
20	5 per cent dextrose.....	129	530	537	404	421
28	2 per cent sodium chloride.....	145	616	520	918	902
29	2 per cent sodium chloride.....	182	454	460	848	1,030
30	2 per cent sodium chloride.....	60	508	577	686	761
38	10 per cent dextrose.....	144	426	410	380	588
39	10 per cent dextrose.....	160	556	517	366	351
40	10 per cent dextrose.....	137	434	519	322	344
	Average.....	139	512	537	531	583

TABLE 6.—*Dilution of the Blood After the Infusions*

Experiment No.	Solution Infused	Total Amount Infused, Cc.	Estimated Blood Volume of Dog,* Cc.	Duration of Infusion, Minutes	Cell Volume, per Cent		Reduction Following Infusion, per Cent
					Before	After	
9	0.7 per cent sodium chloride	950	1,500	30	61	41	33
10	0.7 per cent sodium chloride	2,600	1,480	26	58	44	24
18	5 per cent dextrose.....	2,000	1,520	38	52	38	27
19	5 per cent dextrose.....	1,200	940	8	44	29	34
	Ringer's solution.....	2,500	(See text)	17	29	17	41
20	5 per cent dextrose.....	2,200	1,700	13	59	45	24
28	2 per cent sodium chloride..	2,000	1,380	30	61	35	43
29	2 per cent sodium chloride..	2,000	1,100	36	50	30	40
30	2 per cent sodium chloride..	900	1,500	32	38	32	16
39	10 per cent dextrose.....	2,400	1,500	13	73	51	30
40	10 per cent dextrose.....	2,000	1,460	12	44	33	25
	Average.....	2,075	1,417	26	52	36	32

* The blood volume was estimated to be one tenth of the body weight.

DILUTION OF THE BLOOD AFTER THE INFUSIONS

The cell volume [22] expressed in percentage of the total blood volume was determined before and after each of ten infusions.

21. The blood for the determinations of plasma chlorides was collected under oil and centrifugated as for determinations of carbon dioxide in the plasma. Analysis was then made as in the determinations of the chlorides of the whole blood.

22. The cell volume was determined by centrifugating for thirty minutes equal amounts of blood, drawn before and after the infusion, in a graduated centrifuge tube containing an anticoagulant.

Although this series of experiments is small and the conditions as regards the solution injected and the duration of the infusions are so variable that conclusions cannot be drawn, it is noteworthy that the infusion of 2 per cent sodium chloride solution resulted in a greater dilution of the blood than did the injections of the other solutions.

CHANGES IN THE PULSE RATE AND IN THE BLOOD PRESSURE

Determinations [23] of the arterial blood pressure were made during twelve intravenous infusions. Three determinations were made with each of the four solutions. The pulse rate and blood pressure were recorded before, during and, when possible, after the infusion. The slower pulse rates and lower blood pressures usually followed the larger preoperative doses of morphine.

Fig. 1 (experiment 8, dog 11).—Weight, 11.3 Kg.; 1,500 cc. of 0.7 per cent sodium chloride solution (133 cc. per kilogram) injected in twenty-five minutes; no reactions. *1,* taken at start of experiment: blood pressure, 90 systolic and 80 diastolic; pulse rate, 120. *2,* after eight minutes: blood pressure, 96 systolic and 76 diastolic; pulse rate, 116. *3,* after sixteen minutes: blood pressure, 94 systolic and 80 diastolic; pulse rate, 120. *4,* at end of experiment (twenty-five minutes): blood pressure, 86 systolic and 70 diastolic; pulse rate, 160. In figures 1 to 12 the arrows indicate the points at which the intravenous injections were begun and discontinued.

The most frequent change noted in the pulse rate was a marked acceleration which appeared as soon as the infusion was begun and continued until the conclusion of the injection. This was most notice-

23. A continuous tracing was obtained by means of a mercury manometer connected to a cannula inserted in the femoral artery. The tracings give an accurate record of the systolic pressure. The diastolic pressure is unusually high in several of the tracings, owing to an instrumental error, with a resulting incorrect pulse pressure. The respiratory excursion was frequently accentuated; at times it simulated that of the pulse pressure.

able when the pulse rate was relatively slow at the beginning of the injection. In experiment 38 the rate increased from 54 to 156 after the injection of 144 cc. of 10 per cent dextrose solution per kilogram of body weight in twenty minutes. When the initial pulse rate was above 100 the increase incident to the infusion was less marked. In only one determination (experiment 19) was there a reduction of the pulse rate during the infusion. This dog received 128 cc. of 5 per cent dextrose solution per kilogram of body weight in eight minutes with a fall in the pulse rate from 130 to 124. Eight minutes later a second infusion of Ringer's solution was begun, and 266 cc. per kilogram of body weight was injected in seventeen minutes, with a final pulse rate of 120.

The systolic blood pressure before the infusions varied from 80 to 150 mm. of mercury. Simultaneously with the beginning of the injec-

Fig. 2 (experiment 9, dog 12).—Weight, 15.9 Kg.; 950 cc. of 0.7 per cent sodium chloride solution (60 cc. per kilogram) injected in thirty minutes; no reaction. *1,* taken at start of experiment: blood pressure, 80 systolic and 56 diastolic; pulse rate, 62. *2,* after ten minutes: blood pressure, 80 systolic and 60 diastolic; pulse rate, 70. *3,* after twenty minutes: blood pressure, 80 systolic and 70 diastolic; pulse rate, 90. *4,* at end of experiment (thirty minutes): blood pressure, 80 systolic.

tion there usually occurred a definite increase in the blood pressure. In the majority of the infusions of 0.7 per cent sodium chloride and of 5 per cent dextrose solution this initial rise was followed by a fall in pressure which continued throughout the remainder of the injection. At the conclusion of the infusions of these two solutions, the pressure had returned to a level approximately the same as the preinjection level or slightly lower. The infusion of hypertonic solutions of sodium chloride and dextrose resulted in a more sustained initial rise, and the pressure following the three infusions of 2 per cent sodium chloride solution was definitely higher than before the injection.

The changes in the venous pressure as a result of the infusions were more constant. Each infusion resulted in engorgement of the veins

which persisted for several hours. Puncture wounds in the walls of the veins bled freely, and it was necessary to ligate the openings in the vessels after blood was withdrawn for the second chemical analysis. In experiment 40 a determination of the venous pressure was made by Dr. J. P. Baker Jr. Following the injection of 137 cc. of 10 per cent dextrose solution per kilogram of body weight in twelve minutes, the venous pressure rose from 50 to 480 mm. of water. The systolic arterial pressure fell from 150 to 136 mm. of mercury during the infusion. Six minutes after the conclusion of the infusion the venous pressure was 560 mm. of water and the arterial pressure was 120 mm. of mercury.

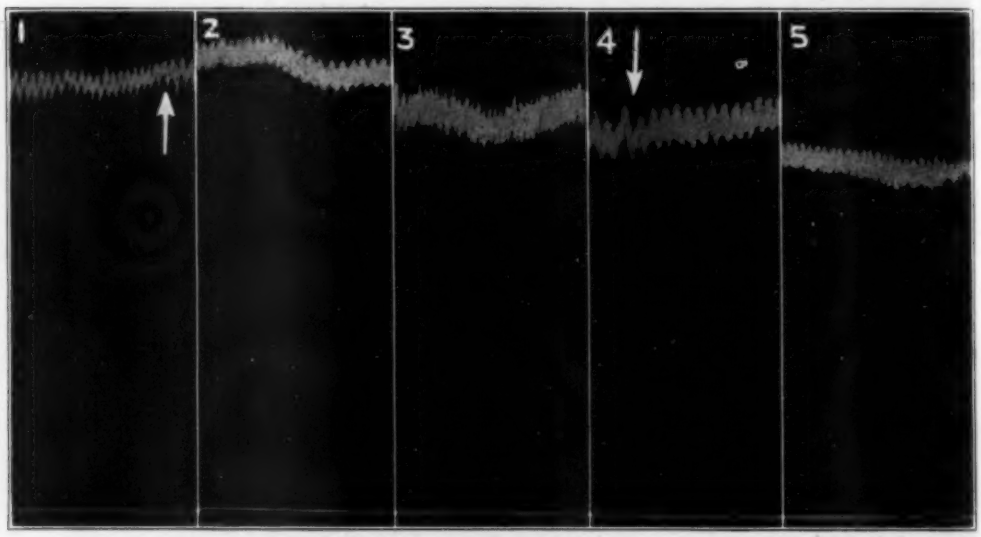

Fig. 3 (experiment 10, dog 15).—Weight, 14.8 Kg.; 2,600 cc. of 0.7 per cent sodium chloride solution (176 cc. per kilogram) injected in twenty-six minutes; no reaction. *1*, taken at start of experiment: blood pressure, 140 systolic and 134 diastolic; pulse rate, 124. *2*, after nine minutes: blood pressure, 146 systolic and 138 diastolic; pulse rate, 150. *3*, after eighteen minutes: blood pressure, 134 systolic and 124 diastolic; pulse rate, 200. *4*, at end of experiment (twenty-six minutes): blood pressure, 130 systolic and 120 diastolic; pulse rate, 200. *5*, seven minutes later: blood pressure, 116 systolic and 108 diastolic; pulse rate, 200+.

RESPONSE TO THE INFUSIONS

The condition of the majority of the dogs at the conclusion of the infusions was satisfactory. All of the animals were obviously larger than at the beginning of the experiment, but, aside from a noticeable clumsiness due to the sudden increase in weight, most of the animals appeared to be unaffected by the infusions. Edema of the subcutaneous

tissues did not appear following any of the infusions. The animals voided freely following the injections. A series of dogs were weighed twelve hours after receiving the injection, and the weight of each animal was found to be less than it had been prior to the infusions.

In one animal pulmonary edema developed. In experiment 19, dog 17 received 1,200 cc. of 5 per cent dextrose solution in eight minutes. The animal was anesthetized with diallyl-barbituric acid. The condition of the dog was satisfactory at the end of the first infusion. After an interval of eight minutes an infusion of Ringer's solution was begun in an attempt to determine the amount of fluid which could be injected before death supervened. The abdomen gradually became distended. This distention increased until respiration became difficult, necessitating

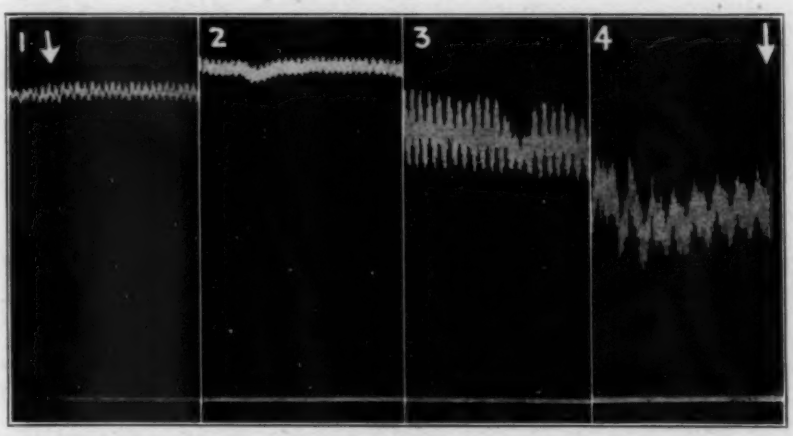

Fig. 4 (experiment 18, dog 16).—Weight, 15.2 Kg.; 2,000 cc. of 5 per cent dextrose solution (132 cc. per kilogram) injected in thirty-eight minutes; no reaction. *1,* taken at start of experiment: blood pressure, 110 systolic; pulse rate, 130. *2,* after twelve minutes: blood pressure, 120 systolic; pulse rate, 116. *3,* after twenty-six minutes: blood pressure, 100 systolic and 90 diastolic; pulse rate, 150. *4,* at end of experiment (thirty-eight minutes): blood pressure, 70 systolic and 56 diastolic; pulse rate, 130.

an incision of the abdominal wall to permit the escape of a large amount of free fluid in the peritoneal cavity. When 2,500 cc. of Ringer's solution had been injected, pulmonary edema developed and the infusion was discontinued. In thirty-five minutes 3,700 cc. of fluid, or 394 cc. per kilogram of body weight, had been injected. The condition of the dog did not change and the pulse rate and blood pressure remained relatively constant until the dog was killed fifteen minutes after the end of the second infusion by the intravenous injection of ether. At autopsy the peritoneal cavity was found to contain a large amount of thin fluid.

The gastro-intestinal tract was filled with fluid and its walls were edematous. The lungs were edematous, but there was no free fluid in the pleural or pericardial cavities.

The dogs receiving injections of 5 per cent dextrose and 0.7 per cent or 2 per cent sodium chloride solution were in good condition at the end of the infusion and showed no unfavorable late symptoms referable to the injection.

In two animals cerebral edema developed following infusions of 10 per cent dextrose solution and death resulted within a few hours. A third dog which received 10 per cent dextrose solution also died soon after the injection.

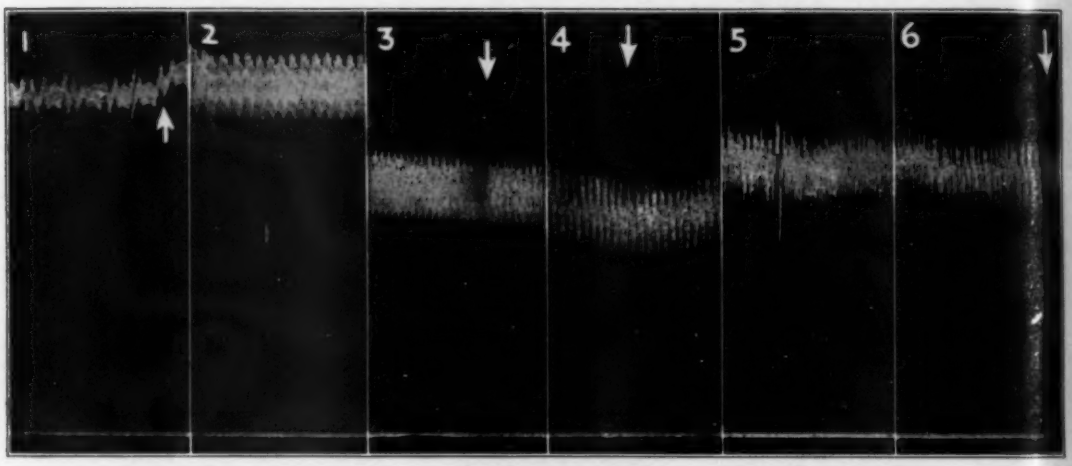

Fig. 5 (experiment 19, dog 17).—Weight, 9.4 Kg. Twelve hundred cubic centimeters of 5 per cent dextrose solution (128 cc. per kilogram) was injected in eight minutes; there was no reaction. After an interval of eight minutes, 2,500 cc. of Ringer's solution (266 cc. per kilogram) was injected in seventeen minutes. Pulmonary edema developed during the latter injection, and the animal was killed fifteen minutes after the end of the second infusion by the intravenous injection of ether. The total amount of fluid, 3,700 cc. (394 cc. per kilogram), was injected in thirty-five minutes. *1*, taken at start of experiment: blood pressure, 116 systolic and 106 diastolic; pulse rate, 130. *2*, after four minutes: blood pressure, 124 systolic and 104 diastolic; pulse rate, 124. *3*, at end of infusion of dextrose solution (eight minutes): blood pressure, 90 systolic and 74 diastolic; pulse rate, 124. *4*, eight minutes later, at start of infusion of Ringer's solution: blood pressure, 80 systolic and 64 diastolic; pulse rate, 110. *5*, after eight minutes: blood pressure, 96 systolic and 80 diastolic; pulse rate, 124. *6*, at end of experiment (seventeen minutes): blood pressure, 90 systolic and 74 diastolic; pulse rate, 120.

ANALYSIS OF THE DEATHS

Three dogs died within twelve hours following the injection. These animals received infusions of 10 per cent dextrose solution.

In experiment 36, dog 7 received 1,800 cc. of 10 per cent dextrose solution (189 cc. per kilogram of body weight) in fifteen minutes. Local anesthesia was used. No insulin was given to convert the 180 Gm. of dextrose contained in the solution, and the blood sugar value was

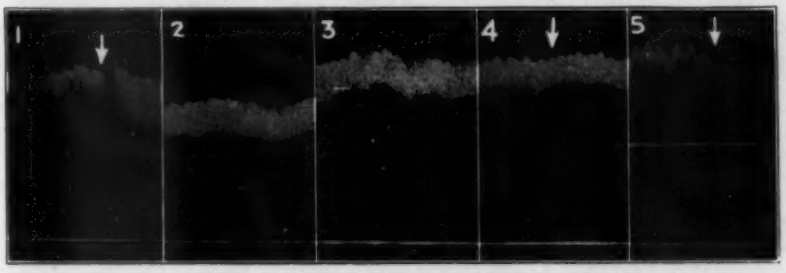

Fig. 6 (experiment 20, dog 21).—Weight, 17 Kg.; 2,200 cc. of 5 per cent dextrose solution (129 cc. per kilogram) injected in thirteen minutes; no reaction. *1*, taken at start of experiment: blood pressure, 80 systolic and 70 diastolic; pulse rate, 104. *2*, after four minutes: blood pressure, 64 systolic and 52 diastolic; pulse rate, 90. *3*, after nine minutes: blood pressure, 82 systolic and 70 diastolic; pulse rate, 116. *4*, at end of experiment (thirteen minutes): blood pressure, 84 systolic and 74 diastolic; pulse rate, 104. *5*, ten minutes later: blood pressure, 88 systolic; pulse rate, 128.

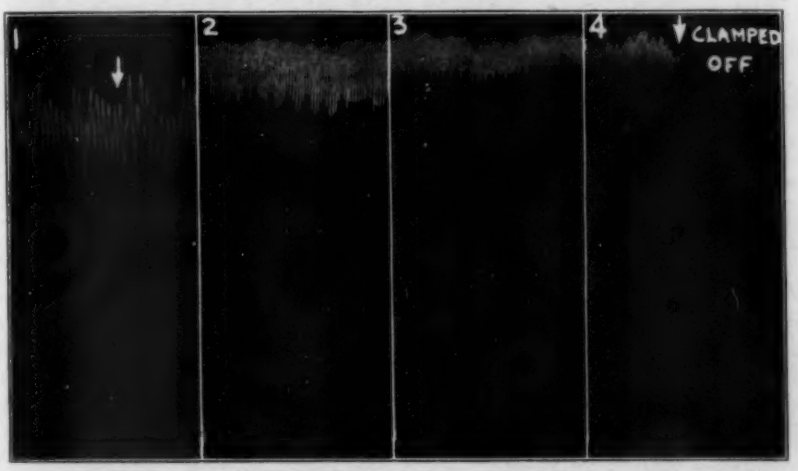

Fig. 7 (experiment 28, dog 13).—Weight, 13.8 Kg.; 2,000 cc. of 2 per cent sodium chloride solution (145 cc. per kilogram) injected in thirty minutes; no reaction. *1*, taken at start of experiment: blood pressure, 116 systolic and 96 diastolic; pulse rate, 54. *2*, after ten minutes: blood pressure, 138 systolic and 118 diastolic; pulse rate, 104. *3*, after twenty minutes: blood pressure, 138 systolic and 128 diastolic; pulse rate, 112. *4*, at end of experiment (thirty minutes): blood pressure, 138 systolic and 130 diastolic; pulse rate, 110.

1,670 mg. per hundred cubic centimeters after the injection. After the injection of 1,500 cc. of solution the dog made slight convulsive movements which continued until the end of the injection. At the conclusion of the infusion the respirations suddenly became slow and shallow and the pulse rate increased from 88 to 140 per minute. A series of convulsions followed which continued until the animal died three hours later. At autopsy the stomach was found to be greatly dilated and the lungs were edematous. There was marked edema of the walls of the stomach and the intestine. A small amount of fluid was present in the peritoneal cavity.

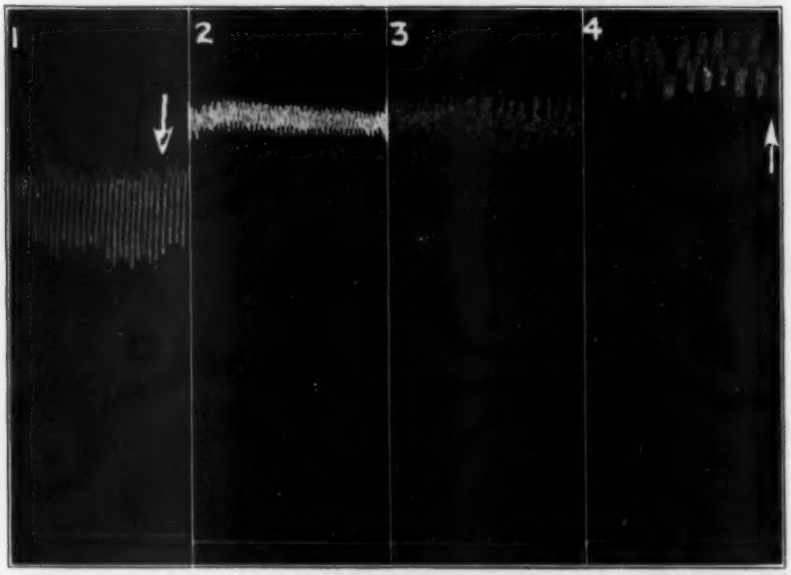

Fig. 8 (experiment 29, dog 14).—Weight, 11 Kg.; 2,000 cc. of 2 per cent sodium chloride solution (182 cc. per kilogram) injected in thirty-six minutes; no reaction. *1,* taken at start of experiment: blood pressure, 112 systolic and 88 diastolic; pulse rate, 64. *2,* after twelve minutes: blood pressure, 136 systolic and 128 diastolic; pulse rate, 168. *3,* after twenty-four minutes: blood pressure, 136 systolic and 126 diastolic; pulse rate, 160. *4,* at end of experiment (thirty-six minutes): blood pressure, 154 systolic and 144 diastolic; pulse rate, 164.

In experiment 39, dog 20 received 2,400 cc. of 10 per cent dextrose solution (160 cc. per kilogram of body weight) in thirteen minutes. The dog was anesthetized with ether. Two hundred units of insulin was given to convert the 240 Gm. of dextrose contained in the solution. The blood sugar value, which was 240 mg. per hundred cubic centimeters at the beginning of the infusion, rose to 474 mg. at the end of the injection. The dog made several convulsive movements during the

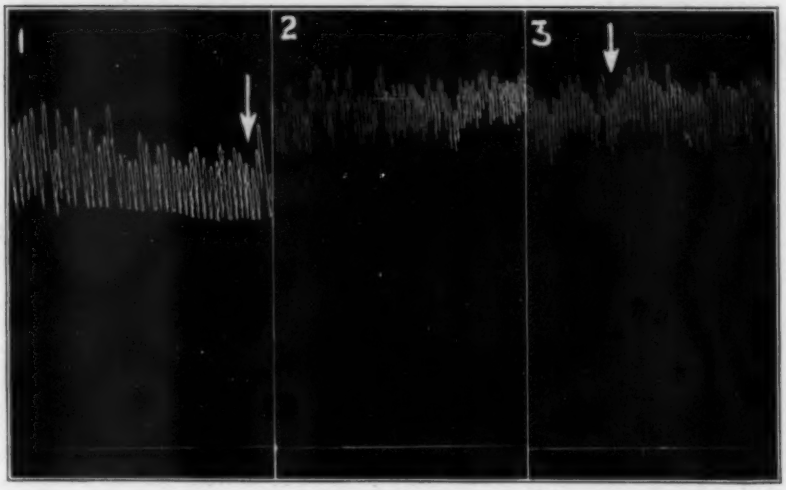

Fig. 9 (experiment 30, dog 12b).—Weight, 15 Kg.; 900 cc. of 2 per cent sodiom chloride solution (60 cc. per kilogram) injected in thirty-two minutes; no reaction. *1,* taken at start of experiment: blood pressure, 94 systolic and 76 diastolic; pulse rate, 50. *2,* after sixteen minutes: blood pressure, 114 systolic and 100 diastolic; pulse rate, 110. *3,* at end of experiment (thirty-two minutes): blood pressure, 116 systolic and 100 diastolic; pulse rate, 88.

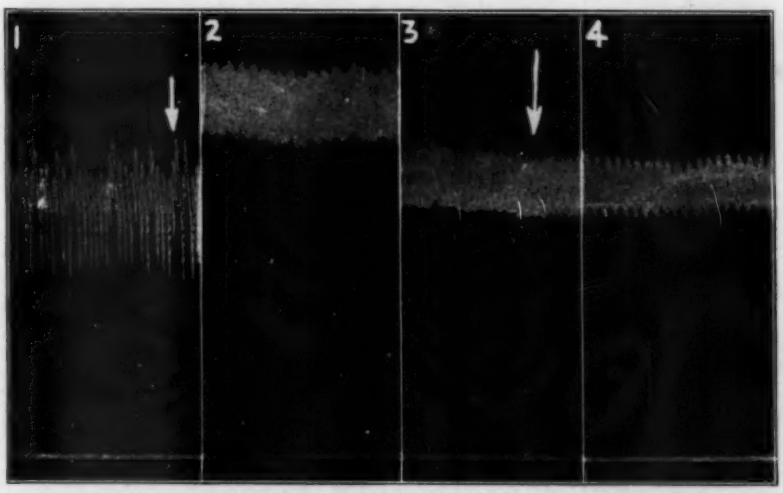

Fig. 10 (experiment 38, dog 19).—Weight, 13.9 Kg.; 2,000 cc. of 10 per cent dextrose solution (144 cc. per kilogram) injected in twenty minutes; no reaction. *1,* taken at start of experiment: blood pressure, 104 systolic and 78 diastolic; pulse rate, 54. *2,* after ten minutes: blood pressure, 136 systolic and 112 diastolic; pulse rate, 160. *3,* at end of experiment (twenty minutes): blood pressure, 106 systolic and 86 diastolic; pulse rate, 156. *4,* fifteen minutes later: blood pressure, 104 systolic and 88 diastolic; pulse rate, 142.

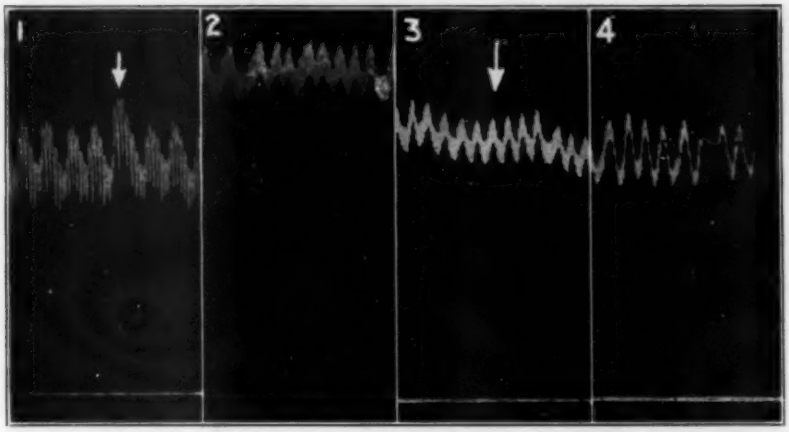

Fig. 11 (experiment 39, dog 20).—Weight, 15 Kg.; 2,400 cc. of 10 per cent dextrose solution (160 cc. per kilogram) injected in thirteen minutes; convulsive twitching during infusion; death within twelve hours. *1,* taken at start of experiment: blood pressure, 90 systolic and 74 diastolic; pulse rate, 86. *2,* after six minutes: blood pressure, 120 systolic; pulse rate, 134. *3,* at end of experiment (thirteen minutes): blood pressure, 92 systolic; pulse rate, 150. *4,* six minutes later: blood pressure, 90 systolic; pulse rate, 150.

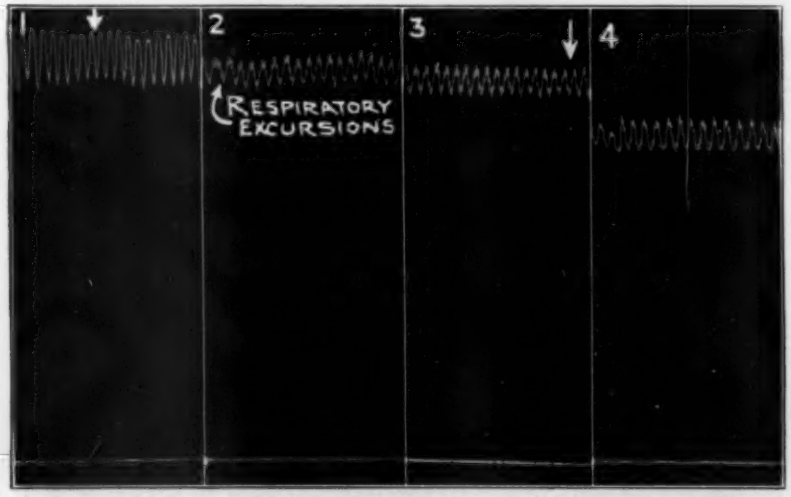

Fig. 12 (experiment 40, dog 22).—Weight, 14.6 Kg.; 2,000 cc. of 10 per cent dextrose solution (137 cc. per kilogram) injected in twelve minutes; marked hemorrhage during experiment; no reaction; death within twelve hours. *1,* taken at start of experiment: blood pressure, 150 systolic; pulse rate, 120 ±; venous pressure, 5. *2,* after six minutes: blood pressure, 140 systolic; pulse rate, 154; venous pressure, 44. *3,* at end of experiment (twelve minutes): blood pressure, 136 systolic; pulse rate, 160 ±; venous pressure, 48 +. *4,* six minutes later: blood pressure, 120 systolic; pulse rate, 150 ±; venous pressure, 56.

infusion but appeared in good condition at the conclusion. The animal reacted from the anesthetic and vomited a large amount of thin fluid. Several hours after the infusion the condition of the dog appeared to be satisfactory, but death occurred during the following night.

In experiment 40, dog 22 received 2,000 cc. of 10 per cent dextrose solution (137 cc. per kilogram of body weight) in twelve minutes. The dog was anesthetized with ether. One hundred and fifty units of insulin was given to convert the 200 Gm. of dextrose contained in the solution. The blood sugar value rose from 159 to 436 mg. per hundred cubic centimeters. The dog lost a larger amount of blood than was usual during the infusion as a result of the manipulations incident to the determination of the arterial and venous pressure. The systolic blood pressure fell from 150 to 120 mm. of mercury during the infusion. The general condition of the animal appeared satisfactory several hours after the infusion, but death occurred during the following night.

SUMMARY

Four series of ten experiments each were made in which twenty-one dogs received intravenous infusions of 0.7 per cent sodium chloride, 5 per cent dextrose, hypertonic sodium chloride and 10 per cent dextrose solutions.

The amount of fluid injected varied from 57 to 394 cc. per kilogram of body weight. The average amount injected for the entire study was 124 cc. per kilogram of body weight. The average duration of the infusions was twenty-four minutes.

The average nonprotein nitrogen content of the blood diminished 7.2 mg. per hundred cubic centimeters following the infusions of 5 per cent dextrose solution, 4.3 mg. following those of 0.7 per cent sodium chloride solution, 0.3 mg. following those of 10 per cent dextrose solution and 0.2 mg. following those of hypertonic sodium chloride solution.

The average blood sugar value increased 19 mg. per hundred cubic centimeters following infusions of 0.7 per cent sodium chloride solution and diminished 23 mg. following infusions of hypertonic sodium chloride solution. The blood sugar value increased markedly following infusions of both 5 and 10 per cent dextrose solution.

The average blood chloride content increased 76 mg. per hundred cubic centimeters following infusions of 0.7 per cent sodium chloride solution and 156 mg. following infusions of hypertonic sodium chloride solution. The average blood chloride content diminished 31 mg. per hundred cubic centimeters following infusions of 5 per cent dextrose solution and 77 mg. following infusions of 10 per cent dextrose solution.

The resistance of the red blood cells to hemolysis was slightly increased following infusions of 5 and 10 per cent dextrose solution;

the resistance was practically unchanged after infusions of hypertonic sodium chloride solution, and there was a slight increase in fragility after infusions of 0.7 per cent sodium chloride solution.

A comparison of the sodium chloride values of the plasma and of the whole blood before and after eleven infusions was not remarkable. The average sodium chloride value of the whole blood before the infusions was 512 mg. per hundred cubic centimeters; after the infusions it was 537 mg., showing an increase of 25 mg. The average sodium chloride value of the plasma before the infusions was 531 mg. per hundred cubic centimeters; after the infusions, it was 583 mg., showing an increase of 52 mg.

Ten dogs with an average estimated blood volume of 1,417 cc. received infusions averaging 2,075 cc. in volume. The average dilution of the blood following the infusions was 32 per cent.

A marked acceleration of the pulse rate occurred during the infusions. The rate gradually returned to normal after the conclusion of the infusions.

A definite rise in the arterial pressure was noted at the onset of the infusions. This initial rise was usually followed by a fall which continued throughout the remainder of the infusion. The secondary fall in pressure was less marked following infusions of hypertonic solutions. After injections of 2 per cent sodium chloride solution the final blood pressure values were higher than at the beginning of the infusions. The venous pressure was markedly increased throughout the infusions.

Pulmonary edema developed in one dog after it had received 394 cc. of fluid per kilogram of body weight in thirty-five minutes.

No dog died following infusions of 0.7 per cent sodium chloride, 5 per cent dextrose or hypertonic sodium chloride solution.

Three dogs died (a mortality of 30 per cent) following injections of 10 per cent dextrose solution. Two of these animals showed signs of cerebral edema; the third lost a large amount of blood during the experiment.

Autopsies on dogs dying after large infusions showed increased fluid in the peritoneal cavity and in the gastro-intestinal tract and edema of the wall of the stomach and the intestine. No fluid was present in the pericardial or pleural cavity. Edema of the lungs was present in two dogs.

COMMENT

The first seven experiments recorded in tables 1 to 4, inclusive, were performed in Germany. The three remaining experiments recorded in each of these tables were performed in this country. A comparison of the nonprotein nitrogen and of the chloride values of the blood in these two groups of dogs should be made. The preinjection nonprotein

nitrogen was uniformly lower in the first than in the second group. The preinjection blood chloride values were uniformly higher in the first than in the second group. These differences were present in each of the four series of experiments in this study.

The changes in the nonprotein nitrogen following the injection of the various solutions in these two groups are as striking as the original differences in the nonprotein nitrogen values. In the first group of dogs with a low nonprotein nitrogen value at the onset, the injection of 5 per cent dextrose solution caused the greatest reduction of the nonprotein nitrogen. In the second group of dogs, with a high nonprotein nitrogen value at the onset, the injection of 5 per cent dextrose solution caused the greatest increase in the nonprotein nitrogen. This reversal of results in the two groups also occurred following the injection of 10 per cent dextrose solution. In the first group of dogs the injection of hypertonic sodium chloride solution resulted in a slight increase in the nonprotein nitrogen. In the second group the injection of hypertonic sodium chloride solution resulted in a decrease in the nonprotein nitrogen. Following only the injection of 0.7 per cent sodium chloride solution were the results in agreement; in both groups the injection of 0.7 per cent sodium chloride solution resulted in a moderate reduction of the nonprotein nitrogen.

A ready explanation for this striking difference is not apparent. A possible explanation is found in the differences in the diet of these two groups of dogs. The diet of the German dogs consisted largely of carbohydrates with little protein. The experiments in this country were performed on dogs accustomed to a diet high in proteins and low in carbohydrates. The high protein diet in the second group may explain the higher preinjection nonprotein nitrogen values and may have resulted in an accumulation of nitrogenous substances in the tissues which appeared in the blood following the increased metabolism caused by the injections of dextrose. The failure of these nitrogenous substances to appear in the blood after the injections of sodium chloride solutions may be due in the same manner to the absence of metabolic activity after the infusion of relatively inert solutions.

The chief difference in the effect of the infusions on the blood chloride values in the two groups was noted following the injection of hypertonic sodium chloride solutions. In the first group of dogs with higher preinjection blood chloride values the infusion of a hypertonic sodium chloride solution resulted in a moderate increase in the chloride values. In the second group with a lower preinjection blood chloride value the infusion of a hypertonic sodium chloride solution resulted in a much greater increase in the blood chloride values. This is in accord with the clinical findings in patients with normal and lowered blood chloride values following the injection of hypertonic salt solution.

A larger amount of fluid proportionately was given in each infusion than would be injected intravenously into a human subject. If the injection of 1,000 cc. of fluid an hour is considered the maximum dose for an adult human being weighing 65 Kg., the average amount of solution injected in this study was equivalent to 8 liters of fluid in twenty-five minutes, or twenty times the amount which would be injected into a human subject in a corresponding time. The largest infusion given in this series without causing untoward symptoms was equivalent to 14 liters of fluid for a human being, or about fifty times the amount of solution which would be injected in a corresponding time. In order to produce pulmonary edema in a dog it was necessary to inject the equivalent of 25 liters of fluid for a human being in thirty-five minutes.

While no dog in this study showed evidence of cardiac embarrassment, it must be remembered that these experiments were performed on healthy animals with normal cardiovascular systems. In actual practice intravenous fluids are frequently needed by debilitated patients with damaged circulatory systems. The purpose of the experiments was to determine the margin of safety attending the intravenous injection of fluids and the changes in the blood which follow the injection of these solutions. The results of these experiments should not be interpreted as justifying the injection of larger amounts of fluid than are given at the present time.

CONCLUSIONS

1. Large amounts of the usual solutions used for infusions may be injected intravenously into dogs without causing death or evidence of cardiac embarrassment. Injections of excessive amounts of fluid result in cerebral or pulmonary edema.

2. The most favorable changes in the blood chemistry occur with infusions of isotonic solutions of dextrose and sodium chloride. A 5 per cent solution of dextrose causes slightly more desirable changes than does a 0.7 per cent solution of sodium chloride. Injections of hypertonic solutions of dextrose and sodium chloride cause distinctly unfavorable changes in the blood chemistry.

3. The blood sugar value increases following infusions of 0.7 per cent sodium chloride solution and decreases following infusions of hypertonic sodium chloride solution.

4. Large infusions of dextrose and of sodium chloride solutions cause little if any change in the fragility of the red blood cells.

5. There is a marked acceleration of the pulse rate during intravenous infusions.

6. The injection of fluids intravenously results in an initial rise in the arterial blood pressure. This is followed by a secondary fall to, or slightly below, the preinjection level during infusions of isotonic solutions. This secondary fall is diminished or absent during infusions of hypertonic solutions.

7. There is a marked increase in the venous pressure during large intravenous infusions.

8. Diuresis is most marked following infusions of 5 per cent dextrose solution.

9. Edema of the subcutaneous tissues does not occur following the rapid injection of large amounts of fluid intravenously. Edema of the wall of the stomach and of the intestine associated with fluid in the gastro-intestinal tract and in the peritoneal cavity does occur following large intravenous infusions.

10. The intravenous injection of 10 per cent dextrose solution results in frequent fatalities in dogs.

The historical references were obtained from articles by Fortescue-Brickdale [1] and Gladstone.[2]

Drs. E. Rehn and H. Widenhorn of Freiburg and Drs. I. A. Bigger, J. C. Forbes, H. B. Haag and C. M. Nelson of Richmond assisted in this study.

PRIMARY ISOLATED LYMPHOGRANULOMATOSIS OF THE STOMACH

REPORT OF A CASE

HARRY N. COMANDO, M.D.
NEWARK, N. J.

Reports of cases of primary isolated Hodgkin's disease of the stomach are sufficiently rare in the literature to warrant the report of another case. Since the time of Billroth, Hodgkin's disease has been definitely placed in the category of medical diseases. The reason that this disease has come to be considered nonsurgical is not so much the technical surgical difficulties entailed as the unfavorable end-results that have followed operative treatment. However, Singer,[1] in a splendid article in 1931, after a careful résumé of the entire literature, cited sufficient evidence to challenge this conception of the disease when the pathologic process is limited to the gastro-intestinal tract. In his article he cited the reports of six cases which he had found in the literature and added one case of his own. A careful search of the literature from 1931 to the present time has failed to disclose any additional cases. At this time I should like to report another authentic case which fully bears out Singer's contention as to the operability and prognosis in such cases.

REPORT OF CASE

History.—Mr. J. S., German, aged 27, was first seen on April 26 1930. For the past three years he had had pain in the epigastrium beginning about three or four hours after meals. The pain was dull, was not relieved by food and radiated to the left side of the chest and to the back. Immediately after eating his abdomen became distended, he belched a great deal, and sometimes vomited. The vomitus consisted of food that had been eaten recently and never contained any blood. The stools had not been bloody. His bowels always moved satisfactorily. His appetite and general health and strength were apparently good. He had lost 15 pounds (7.5 Kg.) during the past year.

Examination.—Physical Examination: The patient was a young man about 5 feet and 7 inches (170 cm.) in height, weighing 120 pounds (54.4 Kg.). His chest, abdomen and extremities were essentially normal. The Wassermann and the Kahn test were negative. Examination of the blood showed 4,550,000 erythrocytes, 80 per cent hemoglobin, 6,500 leukocytes, 60 per cent polymorphonuclears,

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From the Surgical Service of Dr. Harry N. Comando, Newark Beth Israel Hospital.

1. Singer, Harry A.: Primary Isolated Lymphogranulomatosis of the Stomach, Arch. Surg. **22**:1001 (June) 1931.

Fig. 1.—Roentgenogram of the stomach in upright position, showing the characteristic filling defect in malignant infiltration of the pyloric portion of the stomach. The walls of the pylorus are rigid and irregular, and the lumen is narrowed.

Fig. 2.—Roentgenogram of the stomach in horizontal position, showing infiltration of the pyloric portion.

37 per cent lymphocytes, 1 per cent eosinophils, 1 per cent basophils and 1 per cent endothelial cells. The urine was normal except for a faint trace of albumin.

Roentgen Examination (Dr. Nathan James Furst): Examination of the gastro-intestinal tract after the ingestion of a contrast meal showed a medium-

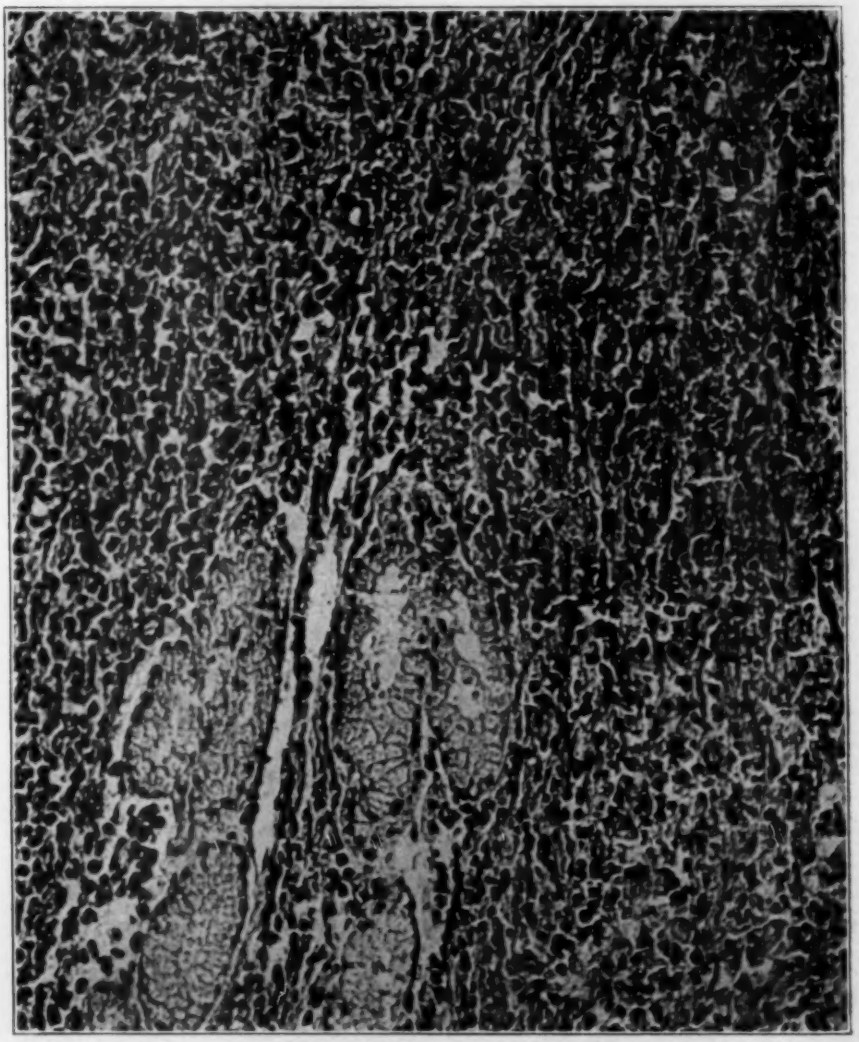

Fig. 3.—Hodgkin's disease (gastric type). Photomicrograph showing lymphogranuloma of the submucosa; × 150.

sized, hypertonic stomach that was active in tone. Its axis was oblique to the lowest point of the greater curvature and about 1 inch (2.5 cm.) below the anterior intersuperior spinous line. The pylorus was situated to the right of the midline and on a level with the fourth lumbar vertebra. Gastric mobility was only fair.

No defect in the pars cardia was noted. In the distal part of the pars media and in a portion of the pylorus a narrowed region was noted for a distance of about 1 inch. The bulbus duodeni was inclined to spasm.

Peristalsis was sluggish. At the point of canalization, no peristalsis was visible. Evacuation was delayed. A small gastric residue remained after six hours, the head of the contrast meal having reached the ascending colon. A tendency to colonic hypermotility was also noted.

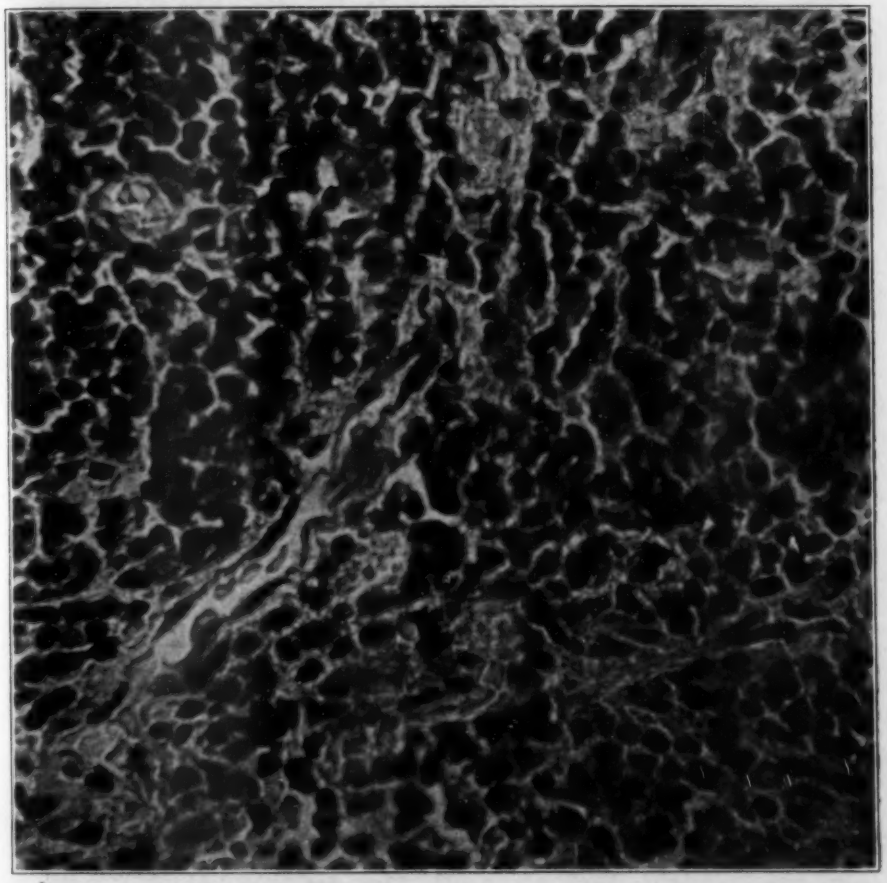

Fig. 4.—Hodgkin's disease (gastric type). Photomicrograph showing extensive granulomatous invasion of the submucosa; × 250.

Summary: The pathologic changes noted were those of an infiltration of the distal portion of the pars media and the proximal part of the pyloric portion of the stomach. A Wassermann test was advised in order to rule out syphilis before an interpretation of the condition as a malignant process was accepted. An increased density was noted in the region of the liver. A small deposit was noted in the lower lobe of the left lung.

Diagnosis: The diagnosis was infiltration of the stomach (providing syphilis was not present).

Operation.—A clinical diagnosis of early carcinoma of the pylorus was made, and the laparotomy was performed on May 6. Under spinal anesthesia, a midline incison was made from the ensiform cartilage to the umbilicus. A mass the size

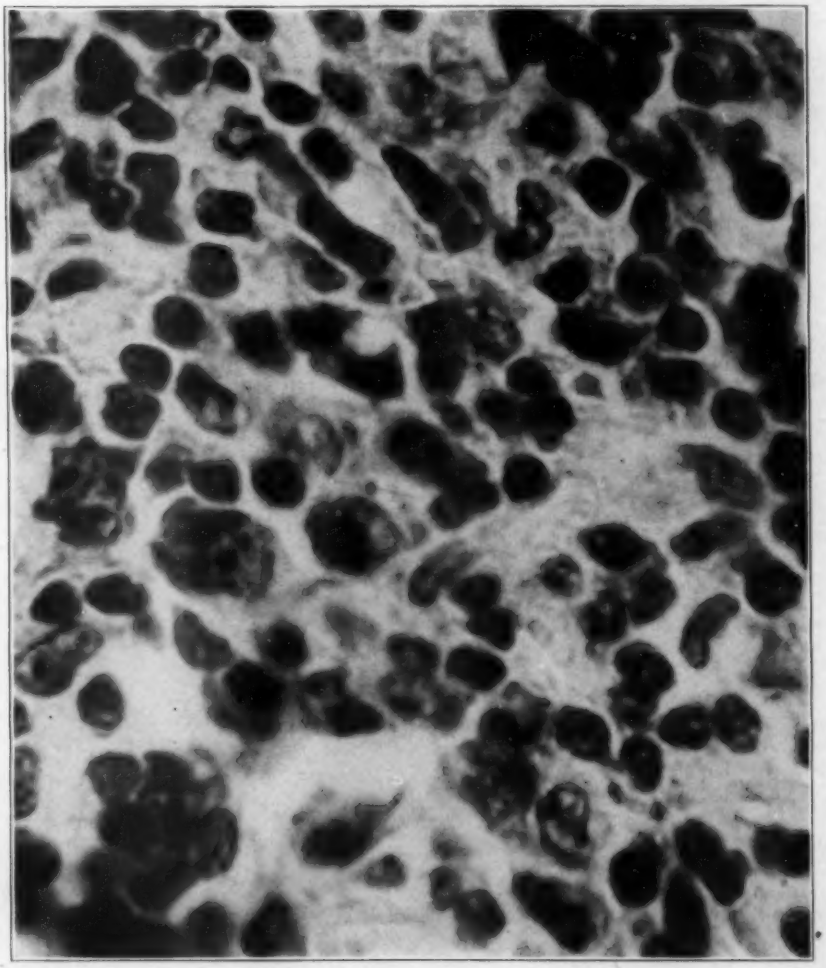

Fig. 5.—Hodgkin's disease (gastric type). Photomicrograph showing lymphoid and epithelioid cells with scattered eosinophils and large multinuclear cells; × 400.

of a 25 cent piece was found on the lesser curvature of the stomach near the pylorus. This mass was pale, rather poorly defined, fairly hard and definitely not inflammatory. Three or four glands the size of a small hazelnut were noted in the lesser omentum. A partial gastrectomy was performed, using Polya's method,

the line of incision on the stomach beginning about an inch below the esophageal opening on the lesser curvature and extending to a point on the greater curvature where the splenic artery reached the stomach. All of the stomach distal to this line, including 1 inch of duodenum, was removed. The anastomosis was retrocolic. The abdomen was closed without drainage.

Pathologic Study (Dr. Asher Yaguda).—Gross Examination: The pylorus and the lower end of the stomach, measuring 10 cm. in length and 4 cm. in width

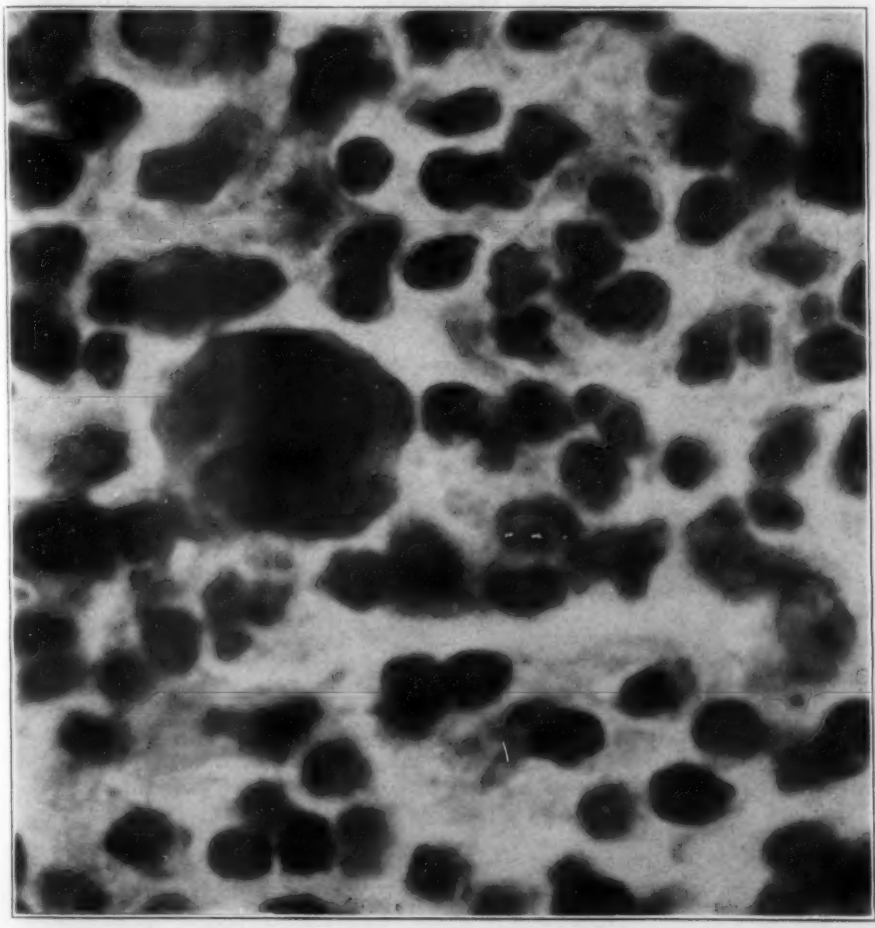

Fig. 6.—Hodgkin's disease (gastric type). Photomicrograph showing lymphoid and epithelioid cells with scattered eosinophils and large multinuclear cells. A large so-called Dorothy Reed cell may be noted; × 774.

were removed at operation. The serosa was smooth and glistening and showed no evidence of scars or of any other pathologic condition. The wall of the stomach was soft and of normal thickness except for an area over the lesser curvature, about 4 cm. in diameter, where it was firmer and felt thickened. On section

through this area, the wall was seen to be markedly thickened, chiefly because of an infiltration in the submucosa. The muscularis, although it was slightly hypertrophied, did not appear to be involved in the process. The mucosa of the stomach was normal in appearance except over the area already described, where definite atrophy and absence of rugae were noted. A few ridges, which appeared to be infiltrated and were definitely indurated, were seen. There was no evidence of ulceration of the mucosa.

Microscopic Examination: Sections which were taken from the area described showed a diffuse infiltration by round cells with dark nuclei which resembled lymphoid cells. Under a high power lens many larger cells were seen, some of which were multinucleated and resembled typical cells of Reed and Sternberg. The

Fig. 7.—Roentgenogram made after resection of the pylorus. There is a well functioning stoma.

glands of the mucosa appeared to be normal, and there was no evidence of epithelial neoplasia. The infiltration was confined to the submucosa and mucosa and did not extend to the muscularis in any of the sections that were studied.

Diagnosis: The diagnosis was Hodgkin's lymphogranuloma.

Postoperative Course.—The patient left the operating room in good condition and made an uneventful recovery. On May 26 a more complete roentgenologic study was made. It showed that there was a well functioning stoma, with no residue after six hours. In the lower lobe of the left lung a small dense deposit was seen, which had the appearance of a calcified gland. The patient was discharged from the hospital on May 29 feeling perfectly well. In two months he

had gained 25 pounds (11.3 Kg.), had returned to his usual occupation, that of a helper on a farm, and was able to eat all kinds of food. A careful follow-up has shown no evidence of any recurrence and the patient continues to feel perfectly well.

CONCLUSIONS

1. Hodgkin's disease may originate in the lymphoid tissue of the gastro-intestinal tract and remain as a localized tumor for some time.

2. The diagnosis usually made is that of carcinoma.

3. Before the days when gastric resection was the operation of choice for gastric tumors and for infiltrating gastric ulcers, practically no cases similar to this one were reported in the literature.

4. This type of gastric lesion is a distinct clinical entity, and the favorable results which have followed operative treatment in several cases more than justify the radical operation.

CONGENITAL ABSENCE OF PENIS

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The early literature rarely mentions congenital absence of the penis. The condition is extremely unusual. We have been able to collect only seven genuine cases in a review of the literature after 1700, although there are many examples of pseudohermaphrodism, rudimentary penis, concealment of the penis behind an abnormal duplicature of skin, hypospadia and similar abnormalities.

Saviard's report in 1702, describing "a child without a penis," is interesting:

> The court surgeon at Sens wrote me during the month of January 1701, that a woman of the parish of Saint Pierre le Rond in that city had been delivered a short time previously of a child who had no penis, but instead only a small, slightly flattened eminence similar to the rump of a hen—above and alongside of which there was some fungous flesh the size of a silver crown, and a finger-width thick, round and elevated; and that the umbilicus was not in the middle of the abdomen—but above the pubes, very close to this fungous flesh.
>
> The small eminence had two little perforations through which urine was discharged. He further stated that when the mother was questioned concerning this phenomenon, she answered that it might well be the result of the great desire she had during pregnancy to eat a chicken, because having bought one which was found to be diseased, she had been very much disappointed at not being able to satisfy her appetite.

Dufour's patient, aged 43, presented congenital tabes, complete blindness, slight nystagmus and the following congenital anomalies: a penis reduced to the size of the clitoris and surmounted by a stout cap; a fat pad resembling the labium majus on each side of the penis, double inguinal hernia, scanty development of hair, bilateral testicular atrophy, harelip, cleft palate and abnormal implantation of the teeth with the incisors in two parallel rows. Goddard's patient, born dead, had congenital absence of one leg and of the foreskin of the penis. Atkinson reported the case of a man, aged 40, who was normal with the exception of congenital absence of the glans penis. In one instance reported by Vance the corpus spongiosum was congenitally absent and was replaced by an unyielding fibrous cord. Erections resembled chordee. The left testis was atrophic, and the right one was smaller than normal. In Lemke's patient, a child 5 months of age, the penis was found beneath the scrotal skin, with the urethra emptying at the lower anterior por-

tion of the scrotum. Green, in 1879, reported the birth of a child in whom the penis was absent anteriorly as though amputated by a sharp instrument cutting forward and upward from the penoscrotal angle.

In true congenital absence of the penis the urethra has opened in or above the anus or through the perineum. Most often the urine was passed just within the anus. Complicating the discharge of urine by rectum, excoriation and ulceration developed about the anus in two of the adults. One patient anointed himself about the anus to prevent

Fig. 1.—Total absence of the penis in a boy, aged 13, of average size and weight.

irritation. Burning and itching in the rectum were troublesome in the adults and these symptoms were accompanied by chills, fever, sweats and weakness, apparently due to urinary sepsis. Though the testes were normally formed, orchitis occurred in one instance.

Two patients were infants, another was a child of 7 years and three were adults. One of the adults (Räuber, 1890) presented a small erectile eminence below the urethral opening in the anus; during sexual excitement this became swollen, and semen passed into the rectum.

Epileptic convulsions were present until the age of 30, and toxic goiter developed at the age of 38. In another adult (Göschler, 1859) there was an erectile mass on the perineum in front of the anus. Excitement

Fig. 2.—Normally formed scrotum and testis. There was no hernia or hydrocele. The raphe was present anteriorly.

Fig. 3.—Normal perineum and anus. The anterior end of the raphe is indicated by the forceps.

produced by friction over this tissue induced orgasm and a discharge of semen into the anus. Death occurred in one instance at the age of 30. This was due to infection of the kidney following a simple operation for hemorrhoids; the man had been married several years.

It will be noticed that in even the seven collected cases of true congenital absence of the penis, additional anomalies complicated the picture

Fig. 4.—Absence of the raphe from the posterior aspect of the scrotum.

Fig. 5.—The upper forceps points to a cicatricial mark at the end of the scrotal raphe. The raphe is absent between the points indicated by the forceps.

often. Thus, erectile tissue occurred on the perineum in one patient and inside the anus in another; epilepsy was present in one adult, and Néalton's patient (1854), an infant, had hydrocele on the left side.

The following case is one of true congenital absence of the penis, remarkable because of the absence of symptoms and the lack of accompanying anomalies.

REPORT OF A CASE

W. C., a 13 year old white boy, was referred to us by Dr. Moccabee of Cardington, Ohio, in January 1931. His parents stated that he had been born without a penis. There was otherwise nothing significant in the history. The child had been healthy, had played as other children of his age and had never presented symptoms

Fig. 6.—Roentgenogram taken sixty minutes after injection of dye intravenously. The bladder is outlined in front of the sacral promontory. The ureters are visualized. The dye has entered the rectum below the bladder.

suggestive of urinary infection. Urine was voided through the rectum, but the child was unable to distinguish the desire to defecate from the call to pass urine. The parents observed that, though this boy had three or four bowel movements a day, the stools were often liquid and quite clear.

On physical examination the boy appeared healthy and normal except for total absence of the penis. His physical and mental development and his manner were about the same as those of the average boy of his age. The changes of puberty had not yet occurred. Close examination of the scrotum and perineum revealed

not the slightest trace of a vestigial penis or other rudimentary structure suggesting a penis. The scrotum was normally formed, and contained two normal, fully descended testes, and the spermatic funiculus and vas were palpable as usual on each side. There was no hydrocele or hernia. The right testis was placed somewhat lower in the scrotum than the left. The raphe was absent from the posterior aspect of the scrotum and extended only 1 inch (2.5 cm.) anteriorly from the anus onto the perineum. The raphe on the anterior scrotal wall terminated in a small cicatricial mark at the dependent portion of the sac. The anus was entirely normal, and there were no ulcers or excoriations in this region.

Proctoscopic examination revealed no trace of a urinary orifice near the anus, but urine was seen to trickle along the anterior wall of the rectum. The opening

Fig. 7.—Roentgenogram taken thirty minutes following the injection of iopax. The fusiform sacculation of each ureter is seen opposite the fifth lumbar vertebra.

was apparently small and hidden in an anterior fold of rectal mucosa. Urography after intravenous injection of iopax disclosed the presence of bilateral hydro-ureter, most marked opposite the fifth lumbar vertebra. Each ureter presented a sacculation at this level. The pelves of the kidney were fairly visible and moderately dilated. The bladder outlined by the dye lay opposite the sacro-iliac joints and extended upward to the middle of the fifth lumbar vertebra. No urethra could be visualized. We advised against ureteral catheterization and cystoscopy because of the likelihood of producing urinary infection.

SUMMARY

True congenital absence of the penis is extremely rare. In the seven cases previously recorded accompanying congenital defects were common,

and ectopic erectile tissue was often noted. It is probable also that hydro-ureter and hydronephrosis would have been frequently observed in these instances had the present methods of urologic investigation been available. So far as we can determine, this is the first time such a patient has been studied by urography following intravenous injection. The case is particularly unusual because examination revealed no other external abnormalities.

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EFFECTS OF LOCAL IMMUNIZATION ON THE DEVELOPMENT OF EXPERIMENTAL ABSCESSES OF THE LUNG

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The development of experimental methods for the production of abscesses in the lungs of dogs has contributed materially to the knowledge of the pathogenesis, complications and treatment of similar infections in man, but information as to means of prevention is still rather meager. This study deals with the preventive phase of the problem and presents data which justify the hope that localized infections of this sort can to some extent be prevented, or at least that their ill effects can be lessened.

An adequate understanding of the ways by which the lungs prevent or resist the progress of infectious agents within them depends on a proper recognition of their structural and functional characteristics under both normal and abnormal conditions. The remarkable extent to which the lungs of the average city dweller filter out and retain coal dust and the infrequency with which such particles are disseminated through the blood stream indicate the presence of an unusually efficient barrier to the hematogenous distribution of particulate exogenous agents. As the progress of inhaled materials must end in the smallest units of pulmonary structure, the alveoli, the principal barrier is evidently the alveolar wall. This wall consists of reticulum, collagen and capillary endothelium and is lined by or contains within it the alveolar macrophages or septal cells. Although the origin of these cells is uncertain, pathologic and experimental evidence reveals that they have definite phagocytic proclivities while they are attached to the septum or while they are free in the alveolar spaces. Particles entering the alveolar spaces must therefore necessarily come in contact with many of these cells, and the numbers and phagocytic potentialities of the latter will determine, to a large extent, the fate of the particles. Experimental evidence supports this view. For example, foreign corpuscles

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(Briscoe [1]), bacteria (Fried [2]) and such materials as india ink, trypan blue and carmine (Sewell,[3] Foot,[4] Gardner and Smith,[5] Lang [6] and Fried [7]) when injected intratracheally are engulfed primarily by the pulmonary macrophages, and comparatively small amounts directly enter the blood stream.

A similar barrier effect presumably occurs when living bacteria are inhaled, and the well known primary complex in tuberculosis illustrates the ability of the lungs to localize the tubercle bacilli of the first infection. The earliest stage of the localizing mechanism probably consists in the adherence of the bacteria to the wall of the alveolar septum or their early engulfment by macrophages or leukocytes within the lungs. Although the ultimate fate of the micro-organisms depends on their ability to grow within the affected tissues or cells, the essential initial conflict is between the invading bacteria and the pulmonary phagocytes.

This early local phagocytic reaction suggests that conditions of local immunity may modify the extent of exogenous pulmonary infection. Several investigators, indeed, have obtained evidence for the existence of a local pulmonary immunity. For example, animals immunized intratracheally with killed diphtheria bacilli have acquired a resistance to many lethal doses of the homologous living organism subsequently introduced intratracheally, although animals used as controls, which were subcutaneously immunized, died after similar intratracheal injections. Conversely, animals immunized intratracheally were not protected against intravenous injections of live diphtheria bacilli (Besredka [8]). Pfenninger [9] demonstrated that rabbits may be ten times as resistant to the intratracheal injection of living paratyphoid bacilli

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as to the intravenous injection of approximately equal numbers of the same organism. Cecil and Steffen [10] obtained complete immunity to pneumococcic pneumonia in monkeys immunized intratracheally with a pneumococcus vaccine, although the blood serum failed to protect mice against the intraperitoneal injection of small quantities of the culture. Similarly, Jones [11] showed that intratracheal immunization of rabbits with a killed culture of Bacillus avisepticus protected them against intratracheal injection of amounts of living culture invariably fatal for normal rabbits. An increased pulmonary resistance to pneumococci introduced into the lungs of rabbits rendered immune by the previous intratracheal administration of a heat-killed vaccine of the homologous organism has been observed by Stuppy, Cannon and Falk.[12] More recently Burt, Tuttle and Cannon [13] have demonstrated that the efficiency of the pulmonary barrier can be markedly enhanced by intratracheal immunization, as shown by the decreased tendency to invasion of the blood stream when virulent pneumococci are introduced intratracheally. Coggeshall and Robertson [14] have shown that experimental lobar pneumonia produced in dogs which have recently recovered from pneumonia is characterized by resistance to a significantly larger infecting dose than the normal animal can withstand and by a decreased tendency to invasion of the blood stream. These experiments suggest that the pulmonary tissues, when stimulated by local contact with antigen, acquire a greater ability to resist and overcome subsequent infections. This does not imply, however, that general agencies do not also participate in the process. The following experiments were performed in an attempt to secure additional information as to the effects of local pulmonary immunization on the course and development of experimental pulmonary abscesses in the dog.

METHODS

Dogs weighing from 12 to 15 Kg. were used. All of the animals were isolated in clean kennels for from seven to ten days, and those in which signs of distemper developed were discarded.

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Ninety-seven dogs were used, twenty-two of which were for such preliminary work as the determination of the proper time of rest between vaccination and embolization and the optional number of vaccinations. This paper describes the results obtained in seventy-five dogs, divided into four series as follows:

		Number of Animals
Series 1	Intratracheally immunized (specific)	33
Series 2	Intratracheally immunized (nonspecific)	4
Series 3	Subcutaneously immunized (specific)	5
Series 4	Normal control animals	33

Vaccines of Staphylococcus aureus and Bacillus coli were prepared as follows: Kolle flasks containing blood agar were inoculated and incubated at 37 C. for twenty-four hours, after which the growth was suspended in a sterile 0.85 per cent solution of sodium chloride containing 0.3 per cent by volume of a 37 per cent solution of formaldehyde. This type of vaccine was used because of the probability of less denaturization of the antigen complex. The vaccine was kept in the icebox for from three to four days or until it was sterile; it was then centrifugated, and the sediment was resuspended in twice the amount of sterile 0.85 per cent solution of sodium chloride.

In these experiments two bacterial strains were used: (1) a culture of Staph. aureus isolated from the clavicle of a boy suffering from multiple foci of osteomyelitis; (2) a culture of B. coli isolated from the kidney of a man acutely ill with pyonephrosis. Proper virulence of both cultures was secured by serial inoculations into the abdominal wall of dogs until abscesses were regularly produced at the site of injection. The virulence of the bacteria was sustained by recovering the micro-organisms from the pulmonary abscesses produced in the course of the experiments.

The dogs were narcotized withh morphine sulphate (2 grains [0.13 Gm.]) and atropine sulphate (1/75 grain [0.0009 Gm.]) in order to render them quiet for the introduction of the bronchoscope.

The vaccine was sprayed into the main bronchi by means of a special spray tube introduced through the bronchoscope. In some of the animals studied early, as will be noted in table 1, the vaccine was diluted, and from 10 to 20 cc. was introduced into each main bronchus through a long metal tube. In order to avoid the introduction of such large amounts of fluid, the spray method was used in the animals studied later. As a rule, two vaccinations were sufficient to establish a definitely increased resistance, but in the earlier series four inoculations were given at intervals of from three to four days.

The method of Holman, Cutler, Weidlein and Schlueter,[15] for the experimental production of pulmonary abscesses had certain disadvantages in this study: The emboli did not contain the same number of organisms; the wall of the vein was not absorbed after weeks or even months, and the lead shots, as well as the

15. Holman, E.; Weidlein, I. F., and Schlueter, S. A.: A Method for the Production of Lung Abscesses, Proc. Soc. Exper. Biol. & Med. **23**:266 (Jan.) 1926. Cutler, F. C., and Schlueter, S. A.: Experimental Production of Abscesses of the Lung, Ann. Surg. **84**:256 (Aug.) 1926. Weidlein, I. F., and Schlueter, S. A.: Postoperative Lung Abscesses: An Experimental Study, Arch. Surg. **14**:457 (Feb.) 1927. Cutler, E. C.; Schlueter, S. A., and Weidlein, I. F.: Experimental Production of Lung Abscesses, New York State J. Med. **26**:767 (Sept. 15) 1926.

threads used to tie the ends, constituted foreign bodies in the tissues. Furthermore, owing to these foreign bodies, it was impossible to make microscopic sections of an abscess with the embolus in situ.

In a previous paper, one of us [16] described the use of an agar embolus for the production of pulmonary abscesses. This method seemed better suited to the present experiments and was used throughout.

The agar emboli, which contained living bacteria, were introduced into the external jugular vein as follows: The animal was narcotized, and the skin of the left side of the neck was shaved, cleansed and painted with iodine. The skin and the subcutaneous tissue of the neck were infiltrated with 2 per cent

TABLE 1.—*Comparison of the Size of the Abscess Cavity in Normal Dogs and in Locally Immunized Dogs Ten Days After Embolization*

No.	Micro-Organism in Vaccine	Route of Immunization	Micro-Organism in Embolus	Size of Abscess Cavity, Cm.*	Amount of Vaccine, Cc.	Number of Vaccinations	Time of Rest Period, Days
1	Normal	.....	Staph. aureus	0.9	..	..	..
2	Normal	.....	Staph. aureus	1	..	..	..
3	Normal	.....	B. coli	0.8	..	..	..
4	Normal	.....	B. coli	1 by 0.5	..	..	..
5	Normal	.....	B. coli	0.5	..	..	..
6	Normal	.....	B. coli	1 by 0.5	..	..	..
7	Normal	.....	B. coli	1	..	..	..
8	Normal	.....	B. coli	0.7 by 0.5	..	..	..
9	Normal	.....	B. coli	2 by 3	..	..	..
10	Normal	.....	B. coli	0.5	..	..	..
11	Normal	.....	Staph. aureus	0.8 by 0.4	..	..	..
12	Normal	.....	Staph. aureus	0.8	..	..	..
13	Normal	.....	B. coli	0.5	..	..	..
14	Normal	.....	B. coli	0.5	..	..	..
15	Staph. aureus	Intratracheal	Staph. aureus	0.5 by 0.3	40	3	41
16	Staph. aureus	Intratracheal	Staph. aureus	0	40	3	41
17	Staph. aureus	Intratracheal	Staph. aureus	0	40	3	41
18	Staph. aureus	Intratracheal	Staph. aureus	0	40	3	41
19	B. coli	Intratracheal	B. coli	0.2	20	4	23
20	B. coli	Intratracheal	B. coli	0	20	4	23
21	B. coli	Intratracheal	B. coli	0	20	4	23
22	B. coli	Intratracheal	B. coli	0.8	20	4	23
23	B. coli	Intratracheal	B. coli	0	10	2	29
24	B. coli	Intratracheal	B. coli	0	10	2	29
25	B. coli	Intratracheal	B. coli	0	10	2	29
26	B. coli	Intratracheal	B. coli	0	10	2	29
27	B. coli	Intratracheal	B. coli	0.1	10	2	29
28	B. coli	Intratracheal	B. coli	0	10	2	29

* The size of the abscess cavity was determined by measuring from one edge of the cavity to the other; if the abscess was round or almost round, only one dimension appears; if the cavity was oval, two dimensions are given.

0 is the symbol adopted to imply that no cavity existed, and that the embolus was touched on all sides by the surrounding inflammatory tissue, as shown in figure 4.

procaine hydrochloride, a small incision was made, and the external jugular vein was freed from the subcutaneous fat. The vein was incised, and the embolus introduced and washed down with an 0.85 per cent solution of sodium chloride, after which the vein was tied above and below the incision and the skin closed.

The animal was killed by electrocution, and the lungs were removed with the trachea clamped. The tissues were fixed in Zenker's solution which did not contain acetic acid and to which a diluted solution of formaldehyde, U. S. P. (1:10), made neutral, had been added; they were next embedded in celloidin,

16. Tuttle, W. M.: A New Method for the Production of Experimental Abscesses of the Lungs in Dogs, Proc. Soc. Exper. Biol. & Med. **30**:462 (Jan.) 1933.

and sections were cut at from 10 to 12 microns and stained with Maximow's eosin-azure and Mallory's triple connective tissue stain.

In the former stain the celloidin sections, after removal of the celloidin, were stained for twelve hours in a dilute solution of Delafield's hematoxylin and were then stained overnight in a mixture of 10 cc. of 1 per cent water-soluble eosin (Grubler), diluted to 100 cc. with distilled water, and 10 cc. of a 1 per cent aqueous solution of azure 2. The connective tissue stain was Mallory's aniline blue-acid fuchsin-orange G combination, prepared according to the formula given by Mallory and Wright.[16a]

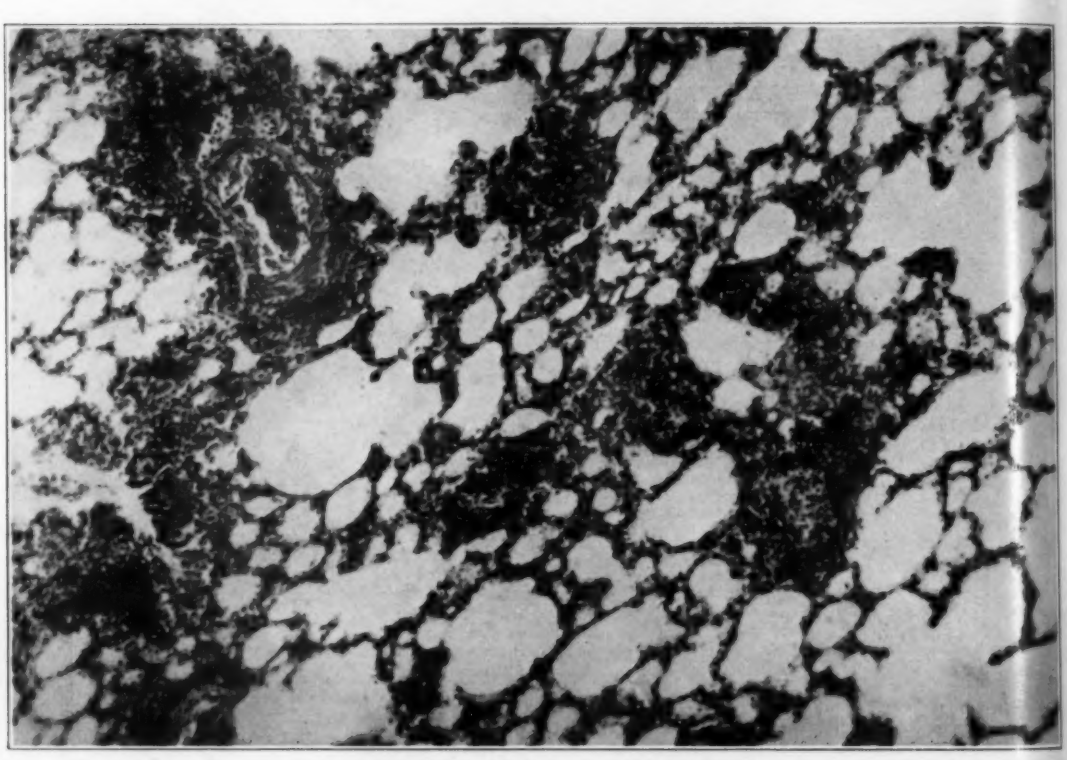

Fig. 1.—Photomicrograph of a section from the lung of a dog vaccinated intratracheally with a vaccine of B. coli killed by formaldehyde. Note the accmulations of basophilic mononuclear cells around the blood vessels; × 88.

EFFECTS OF AN INTRATRACHEAL INJECTION OF A VACCINE CONTAINING FORMALDEHYDE ON THE LUNGS OF NORMAL ANIMALS

In order to determine the changes which may occur in normal lungs following the intratracheal administration of antigen, dogs were immunized by having their lungs sprayed with 6 cc. of a vaccine of B. coli killed with formaldehyde—3 cc. into each main bronchus. One week

16a. Mallory, F. B., and Wright, J. H.: Pathologic Technique, Philadelphia, W. B. Saunders Company, 1924.

later the lungs were sprayed with 4 cc. Eighteen days after this the animals were killed, and the lungs examined grossly and microscopically.

On macroscopic examination the lungs appeared normal. Microscopic examination showed an essentially normal picture except for a slight thickening of the alveolar walls and the presence in the perivascular and peribronchial tissues of a "collar" of basophilic mononuclear cells. This so-called "mantling" (fig. 1) occurred in the lungs of all three animals; it was most marked about the arteries and bronchi but present also about the smaller blood vessels. The cells were large mononuclear cells with deeply staining nuclei. Mitotic figures were seen frequently, and the cells appeared to be multiplying rapidly in situ.

The exact significance of the reaction is uncertain, but presumably it indicates a mesenchymal activation and mobilization of potentially phagocytic cells derived from a local proliferation or a hematogenous emigration of mononuclear cells. It furnishes, however, a morphologic basis for the assumption that increased numbers of these cells may aid in elevating the resistance of the lungs both through their maturation into phagocytes and through their presumed ability to participate in the formation of antibodies.

A COMPARISON OF THE REACTIONS OF NORMAL AND IMMUNE LUNGS TO THE INTRODUCTION OF AN EMBOLUS INFECTED WITH THE HOMOLOGOUS ORGANISM

Fourteen healthy dogs were immunized as described earlier—four with a Staph. aureus vaccine, and ten with a vaccine prepared from B. coli. Four of the animals (dogs 15, 16, 17 and 18) were immunized at intervals of from three to four days by the introduction through a long metal tube on three occasions of 20, 10 and 10 cc., respectively, of the original vaccine diluted 1:10 with a sterile 0.85 per cent solution of sodium chloride. The remaining ten animals received smaller amounts of the original B. coli vaccine introduced into the lungs by means of the spray apparatus. Four vaccinations with 5 cc. each were given dogs 19, 20, 21 and 22, and two vaccinations with 6 and 4 cc., respectively, were given to the remaining six dogs (23 to 28, inclusive). From twenty-three to forty-one days after the last immunization, an embolus infected with the homologous organism was introduced into the external jugular vein. The animals were observed for ten days, after which they were killed and the lungs examined. Fourteen normal dogs were embolized simultaneously with similar emboli and were killed ten days later. The summarized details for this group are given in table 1. The following protocols for a normal control animal and one intratracheally immunized illustrate the typical observations.

Dog 2.—A normal animal was narcotized with morphine sulphate (2 grains) on Oct. 6, 1932, and an embolus infected with Staph. aureus was introduced

into the external jugular vein. On October 7 the animal appeared to be normal; it remained normal until the tenth day, when it was killed by electrocution.

Necropsy.—Autopsy was performed on October 17. The pleural surfaces were smooth and glistening. There were no adhesions or fluid in the pleural cavities. The lungs contained air and were grossly normal except for the presence at the inner margin of the left lower lobe of a mass measuring 3 by 5 cm. When sectioned, the area consisted of a deeply hemorrhagic pulmonary parenchyma containing an abscess cavity 1 cm. in diameter and filled with a thick, yellow pus in which the agar embolus was lying free. The wall was composed of necrotic material, and no definite pyogenic membrane surrounded the abscess cavity.

Microscopic Examination.—Sections taken through the abscess showed that the embolus was missing from the cavity, which was surrounded by a broad zone of polymorphonuclear leukocytes, many of which contained engulfed bacteria, although the number of micro-organisms per leukocyte was few. On one side were many new blood vessels and young fibroblasts. Farther from the cavity were numerous large macrophages containing polymorphonuclear leukocytes and occasional bacteria. There was only a slight fibroblastic reaction at the edge of the leukocytic zone, and the contiguous pulmonary tissue showed little evidence of mesenchymal mobilization.

TABLE 2.—*Comparison of the Size of the Abscess Cavity in Normal, Locally Immunized and Generally Immunized Animals Ten Days After Embolization* *

No.	Micro-Organism in Vaccine	Route of Immunization	Micro-Organism in Embolus	Size of Abscess Cavity, Cm.	Amount of Vaccine, Cc.†	Number of Vaccinations	Time of Rest Period, Days
15	Staph. aureus	Intratracheal	Staph. aureus	0.5 by 0.3	40	3	41
16	Staph. aureus	Intratracheal	Staph. aureus	0	40	3	41
17	Staph. aureus	Intratracheal	Staph. aureus	0	40	3	41
18	Staph. aureus	Intratracheal	Staph. aureus	0	40	3	41
1	Normal	.....	Staph. aureus	0.9	..	..	..
2	Normal	.....	Staph. aureus	1	..	..	..
29	Staph. aureus	Subcutaneous	Staph. aureus	0.2	24	3	41
30	Staph. aureus	Subcutaneous	Staph. aureus	0.8	24	3	41
31	Staph. aureus	Subcutaneous	Staph. aureus	0.6 by 0.3	24	3	41
32	B. coli	Subcutaneous	B. coli	0.3	10	2	45
33	B. coli	Subcutaneous	B. coli	0.7	10	2	45

* The size of the abscess cavity was determined in the manner indicated in table 1.

† The vaccine given subcutaneously to dogs 29, 30 and 31 was a 50 per cent solution of the original vaccine, whereas that given intratracheally to dogs 15, 16 and 18 was a 10 per cent solution of the original vaccine. The vaccine given dogs 32 and 33 was a 50 per cent solution of the original vaccine.

DOG 17.—An immune dog was narcotized with morphine sulphate (2 grains) and atropine sulphate (1/75 grain) on Aug. 18, 1932. Twenty cubic centimeters of a suspension of Staph. aureus killed with formaldehyde was instilled into the lung through a long metal tube—10 cc. into each main bronchus.

Five days later a similar dose of 10 cc. was introduced, and after three days another dose of 10 cc. was given. Throughout the next five weeks the animal remained well.

On October 6 an agar embolus infected with Staph. aureus was introduced into the left external jugular vein; the animal was killed ten days later.

Necropsy.—There was a dark red mass in the lower lobe of the left lung. The overlying pleura appeared to be normal. This mass, when sectioned, consisted of a consolidated area 1.7 cm. in diameter, the outer part of which was a deep red. The inner portion was light, yellowish gray and contained in its center the agar embolus tightly surrounded by inflammatory tissue. No definite cavity caused by an abscess was present.

Microscopic Examination.—The embolus was in place, and at its outer borders the bacterial colonies appeared as dark blue masses, whereas at the center of the embolus the colonies had degenerated and were pale pink. The embolus was immediately surrounded by a narrow zone of polymorphonuclear leukocytes, red blood cells and macrophages. This thin zone was sharply circumscribed by fibroblasts, a few polymorphonuclear leukocytes and many darkly staining mononuclear cells. There were comparatively few bacteria outside the embolus, although small numbers were occasionally seen within the polymorphonuclear leukocytes and macrophages. The blood vessels contained numerous monocytes, and macrophages with a foamy cytoplasm and containing remnants of leukocytes were seen in the

Fig. 2.—Photomicrograph of an abscess present in a normal dog (2) ten days after the introduction into the external jugular vein of an embolus infected with Staph. aureus. Note the large, irregular cavity formed by the abscess and the extensive inflammatory reaction in the surrounding pulmonary tissues; × 7.

contiguous tissues. The area of inflammatory infiltration was sharply circumscribed, and the bacteria were not disseminating.

In general the observations on the lungs of the normal animals were similar to those previously obtained and described by other investigators. An abscess varying from 0.5 to 3 cm. in diameter always formed in the normal animals. The walls of the abscess cavities were ragged, and there was little evidence of healing. Hemorrhagic infarction distal to the abscess occurred frequently. In one animal (dog 9) a large abscess

with a necrotic wall and accompanying massive infarction of the entire lobe had led to perforation, purulent pleuritis and death on the ninth day after embolization.

The microscopic picture (figs. 2 and 3) indicated an advancing rather than a controlled infection. The abscess cavity was surrounded by a leukocytic wall varying from 1 to several millimeters in thickness through which bacteria, both intracellular and extracellular, were scattered. Fibroblasts were numerous only in the abscesses which developed

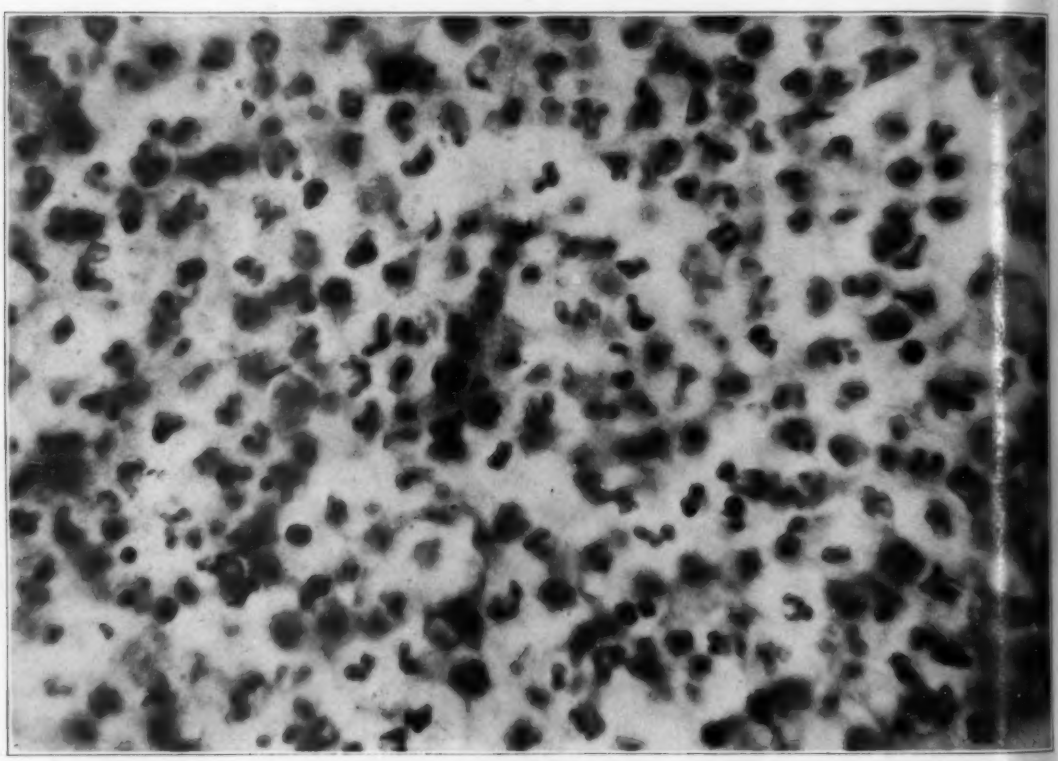

Fig. 3.—Photomicrograph of the wall of the abscess shown in figure 3. Note the predominance of polymorphonuclear leukocytes and the absence of fibroblasts; × 815.

near the larger blood vessels and the bronchi and which appeared to be streaming in from the walls of these structures rather than arising from the mononuclear phagocytes. The mantling reaction was seen occasionally, but not to the extent observed in the immunized animals.

The reactions in the lungs of the immune dogs contrasted sharply with those observed in the normal animals. In only four of the fourteen immune animals did cavitation occur (dogs 15, 19, 22 and 27), and in two of these (dogs 19 and 27) the abscess cavity was small. A large abscess formed in dog 22. As it has been shown that chronic

cough tends to increase greatly the size and chronicity of abscesses in the dog (Van Allen, Cole and Fox[17]), it is of interest that dog 22 coughed considerably before and after embolization.

The embolus in the immune animals was surrounded by a rather dense zone, varying from 2 to 10 mm. in width, of whitish-gray exudate. The average diameter of the abscess cavity in the four of the fourteen immune animals in which cavitation occurred was approximately 0.4

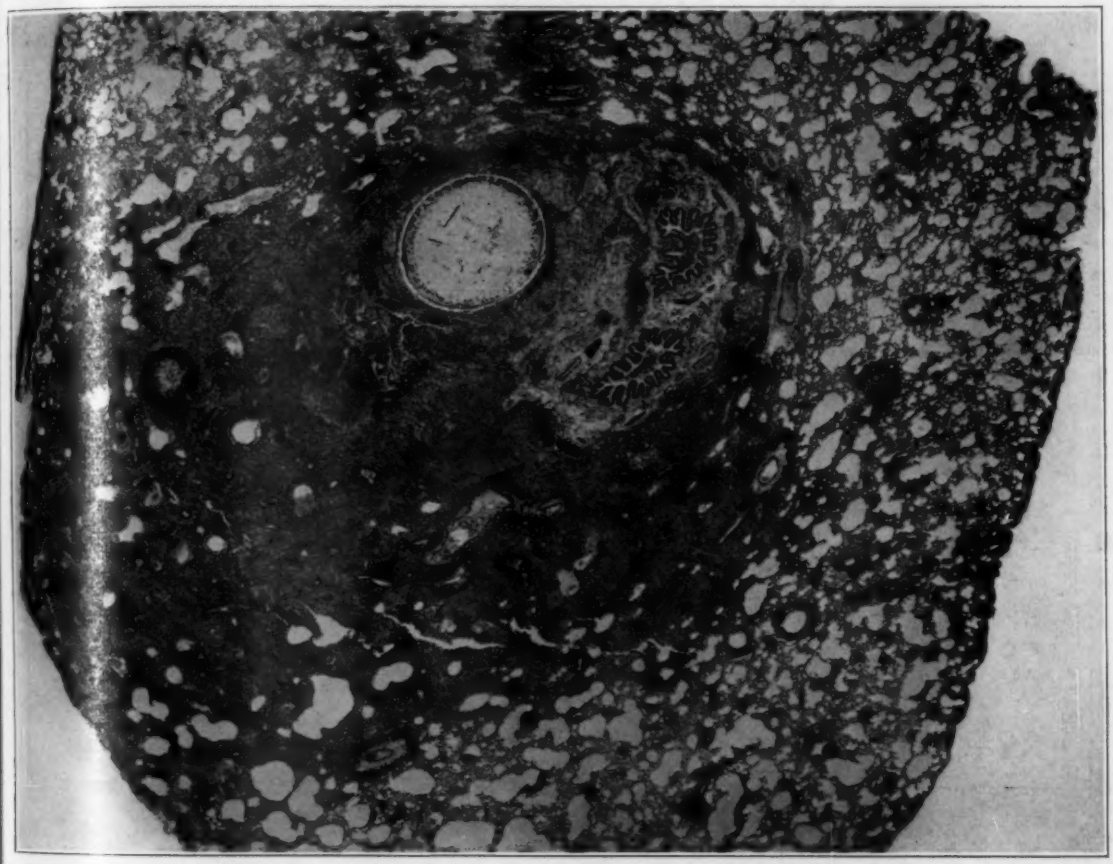

Fig. 4.—Photomicrograph of the abscess about an embolus infected with Staph. aureus in a dog (17) previously immunized by the intratracheal injection of a vaccine of Staph. aureus killed with formaldehyde. Note the relatively small area of pulmonary involvement and the absence of an abscess cavity; × 9.

cm., whereas in the fourteen normal control animals it was 0.85 cm.

In no instance in the immune group did death result from perforation with an ensuing pleuritis.

17. Van Allen, C. M.; Cole, H., and Fox, R. A.: The Influence of Cough on the Chronicity of Lung Abscesses, Proc. Soc. Exper. Biol. & Med. **24**:485, 1927.

The contrast between the abscesses in the two groups was as marked microscopically as grossly (figs. 4 and 5). In general, in the immunized lungs, a narrow zone of polymorphonuclear leukocytes about the embolus was surrounded by a wall of young fibroblasts. Organization of the exudate was distinctly more advanced than in the normal animals; fibroblasts were numerous and tended to encircle the embolus as the healing process advanced. The presence of the fibroblasts appeared to be independent of the existence of large blood vessels or bronchi in

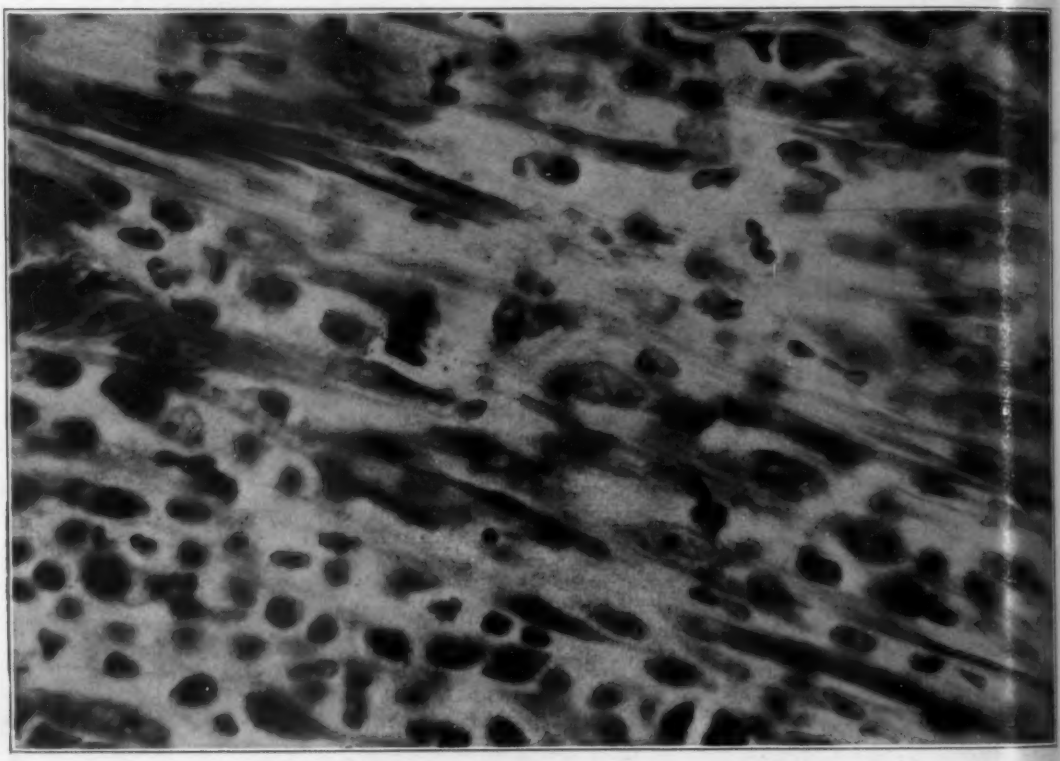

Fig. 5.—Photomicrograph of the wall of the abscess shown in figure 5. Note the fibroblastic reaction; × 815.

the neighborhood of the embolus, suggesting that they may have arisen from macrophages.

Macrophages and large mononuclear cells, frequently containing mitotic figures, were present in greater numbers in the immune than in the normal lungs. Many of the large, foamy mononuclear cells were actively phagocytic, and a considerable number contained polymorphonuclear leukocytes and tightly packed masses of bacteria (fig. 6). In general, fewer bacteria were seen outside the embolus in the immune animals; when present, the bacteria were chiefly within the phagocytic

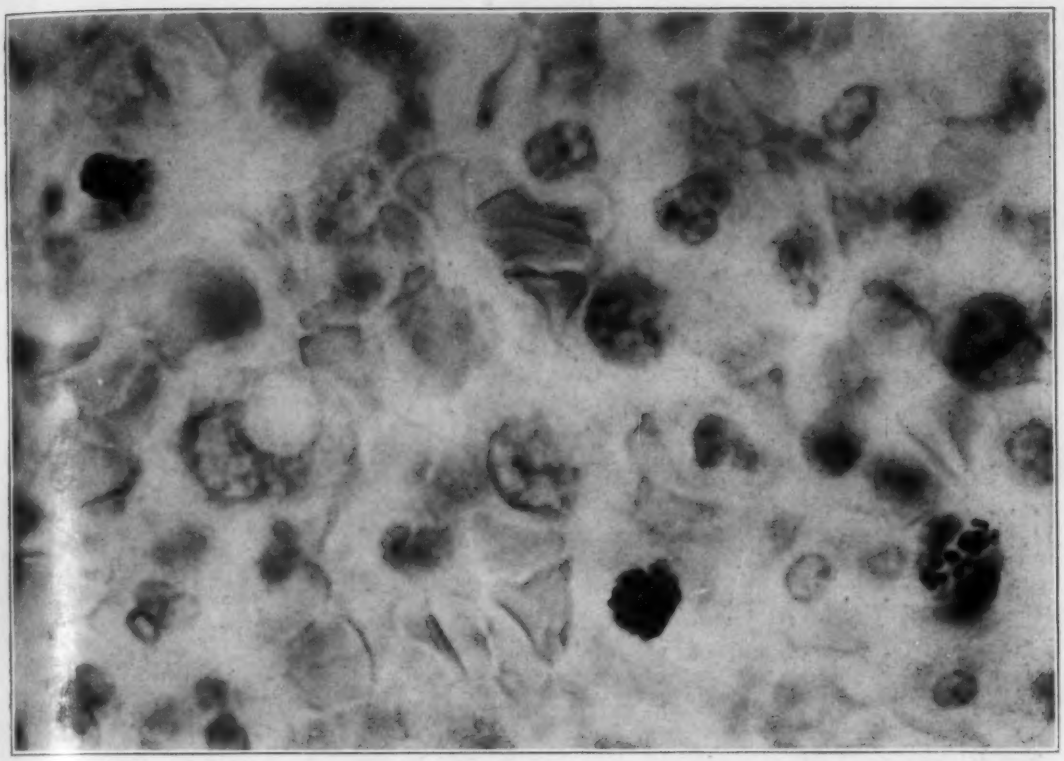

Fig. 6.—Photomicrograph showing the intracellular packing of bacteria within macrophages in the lung of an immune animal; × 1,850.

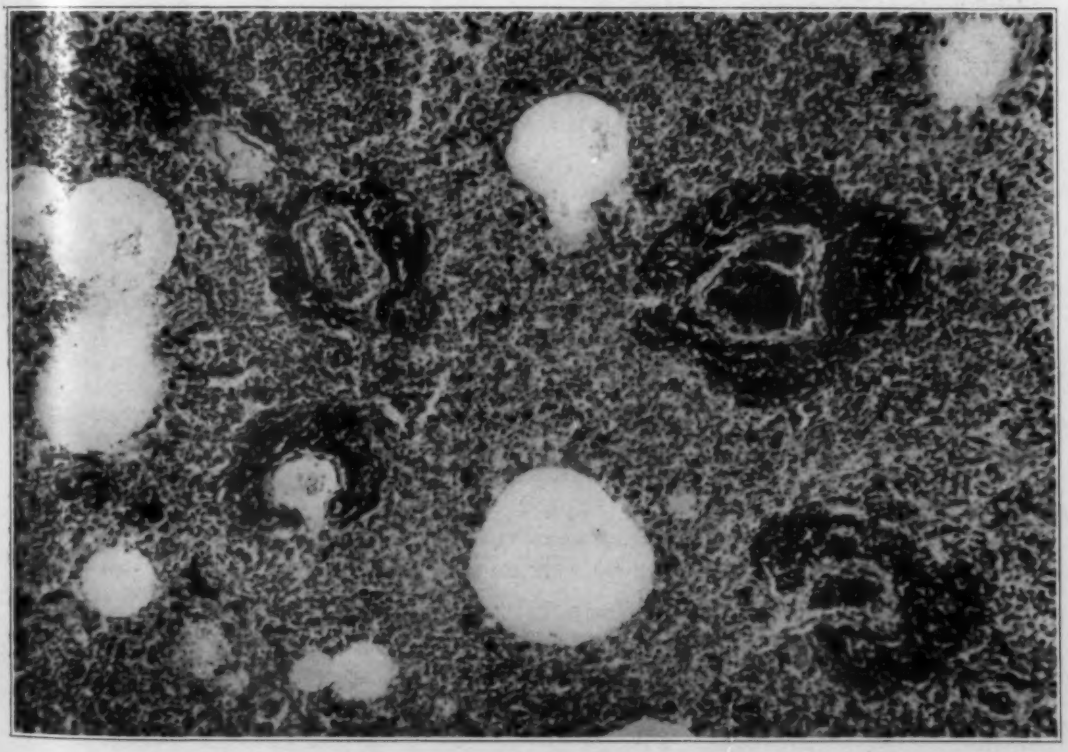

Fig. 7.—Photomicrograph illustrating the perivascular "mantling" in the tissues contiguous to the abscess in an intratracheally immunized dog; × 88.

cells near the embolus. This packing of the bacteria into compact intracellular masses suggests an increased avidity of the macrophages for the bacteria, due presumably to a more intensive bacteriotropic action.

The "mantling" of blood vessels by the large basophilic mononuclear cells (fig. 7) was frequently seen in the inflamed tissues at a considerable distance from the embolus or abscess in the immune animals, a reaction which was regularly more marked than that which occurred in normal control dogs.

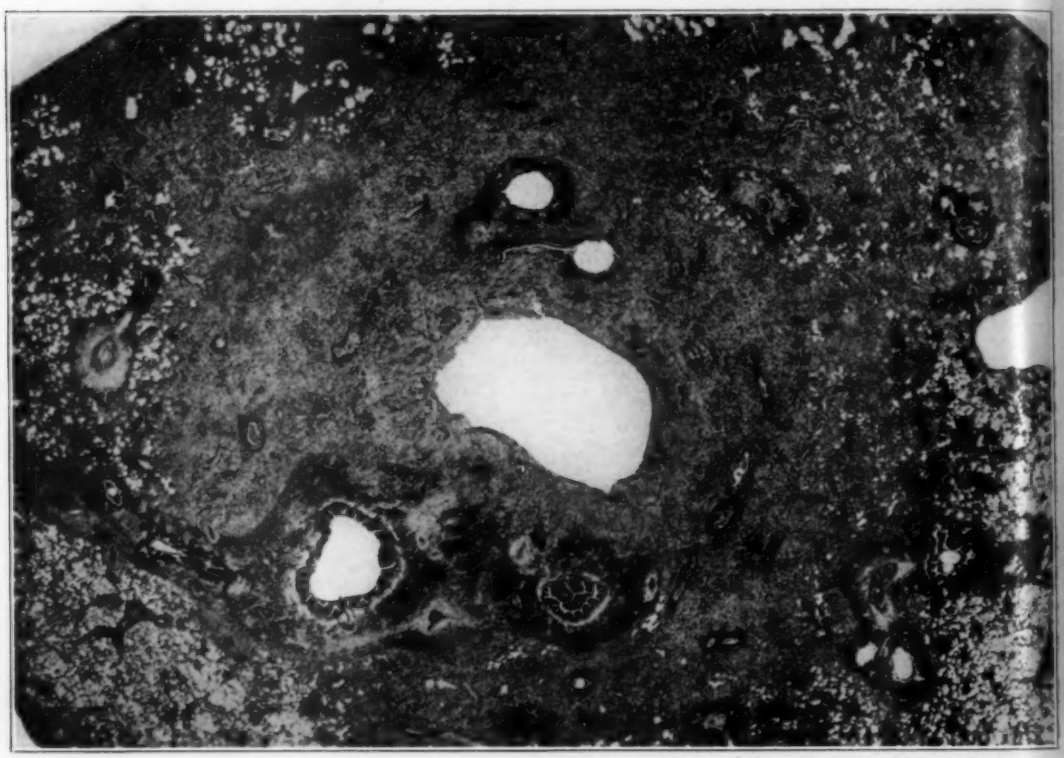

Fig. 8.—Photomicrograph of an abscess of ten days' duration in a dog (30) subcutaneously immunized with a vaccine of Staph. aureus and subsequently infected with an embolus containing the homologous organism. Note the diffuse consolidation of the surrounding pulmonary tissues and the relatively large abscess cavity; × 6.3.

EFFECTS OF LOCAL AND GENERAL IMMUNITY ON THE DEVELOPMENT OF PULMONARY ABSCESSES

Experiments were performed to determine if local pulmonary immunization is more effective than general immunization in restricting the development and extension of pulmonary abscesses. Five healthy dogs were immunized by the subcutaneous injection of a vaccine killed

by formaldehyde, prepared as described in the preceding pages. Dogs 29, 30 and 31 received 8 cc. of a vaccine of Staph. aureus killed by formaldehyde on three occasions at intervals of two days; dogs 32 and 33 received 6 cc. and 4 cc., respectively, on two occasions at intervals of two days. Normal dogs and dogs immunized intratracheally with like amounts of the same vaccine served as controls. After a period of rest following the last vaccination, which varied from forty-one to forty-five days, emboli infected with the homologous micro-organisms

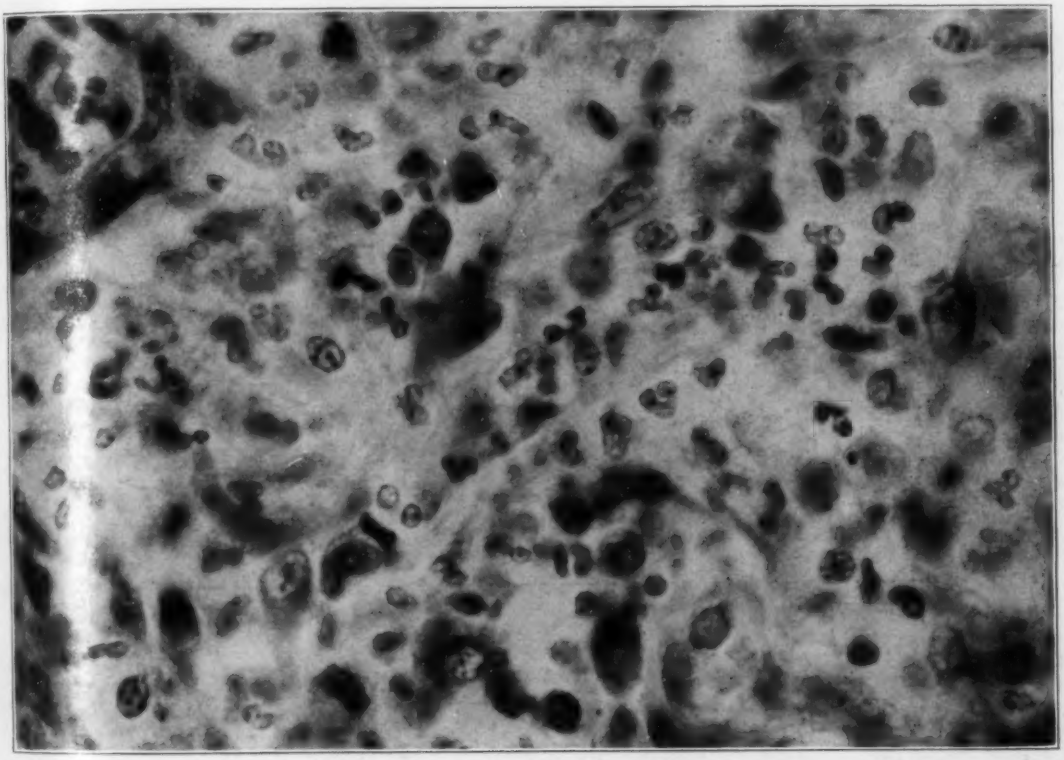

Fig. 9.—Photomicrograph (× 1,815) of the wall of the abscess shown in figure 8.

were introduced. The results obtained in this series are shown in table 2.

As will be seen from an examination of this table and figures 8 and 9, the tissue reactions in the subcutaneously immunized animals ranged in intensity between those of the normal and those of the intratracheally immunized dogs. Organization of the inflammatory exudate in the subcutaneously immunized animals was more vigorous than in the normal dogs, but obviously less than in the intratracheally immunized animals. Cavities were present in the lungs of all the subcutaneously

immunized animals, and in dogs 30, 31 and 33 the diameters of the cavities almost equalled those in the normal controls; this picture contrasts sharply with the small cavities, or the absence of cavities, in the lungs of the intratracheally immunized animals.

COMPARISON OF THE EFFECTS OF SPECIFIC AND NONSPECIFIC LOCAL IMMUNIZATION ON THE DEVELOPMENT OF PULMONARY ABSCESSES

An attempt was made to determine the effects of nonspecific local immunization on the development of pulmonary abscesses. Dogs were immunized intratracheally with a vaccine of B. coli, and pulmonary abscesses were produced later with agar emboli infected with Staph.

TABLE 3.—*Comparison of the Size of the Abscess Cavity in Normal Animals and in Animals in Which Local Immunity Was Effected Specifically and Nonspecifically Ten Days after Embolization*

No.	Micro-Organism in Vaccine	Route of Immunization	Micro-Organism in Embolus	Size of Abscess Cavity, Cm.	Amount of Vaccine, Cc.	Number of Vaccinations	Time of Rest Period, Days
34	B. coli	Intratracheal	Staph. aureus	0.9 by 0.5	10	2	33
35	B. coli	Intratracheal	Staph. aureus	1	10	2	33
36	B. coli	Intratracheal	Staph. aureus	0.2	10	2	33
37	B. coli	Intratracheal	Staph. aureus	0.5	10	2	33
26	B. coli	Intratracheal	B. coli	0	10	2	33
27	B. coli	Intratracheal	B. coli	0	10	2	33
28	B. coli	Intratracheal	B. coli	0	10	2	33
11	Normal	.....	Staph. aureus	0.8 by 0.4	..	..	..
12	Normal	.....	Staph. aureus	0.8	..	..	..
13	Normal	.....	B. coli	0.5	..	..	..
14	Normal	.....	B. coli	0.5	..	..	..

aureus. The summarized proceedings and results are shown in table 3, in which it is seen that abscesses with cavities formed in all four of the nonspecifically immunized dogs, although in one animal (dog 36) the cavity was small.

The microscopic observations on the abscesses in the nonspecifically immunized animals resembled closely those in the normal controls. The bacteria tended to permeate the surrounding tissues, even in the case of dog 36, which otherwise resembled a specifically immunized animal. Phagocytosis, although present about the abscesses, was not marked, and the cells failed to take up the large numbers of bacteria, as previously described in the cases of specifically immunized dogs. Organization of the exudate, as shown by the increased fibroblastic response, was present to a marked degree in only one animal (dog 36), whereas in the others its scarcity resembled the inertia of tissues seen in the normal control animals.

REACTION OF THE IMMUNE AND OF THE NORMAL LUNG TO A SEPTIC EMBOLUS IN THE EARLY AND LATE PERIODS

It was our purpose in this group of experiments to study the lesions produced by the introduction of a septic embolus into the pulmonary tissues of immune and normal control animals, both in the early stages and in the periods after ten days. An embolus infected with B. coli was introduced into the pulmonary artery of twelve intratracheally immunized animals which had received two injections of 6 and 4 cc., respectively, of B. coli vaccine at intervals of seven days followed by a rest period of twenty-one days and of twelve normal animals, and two of the first and two of the second group were killed on the first, second, third, fifth and ninth days after the introduction of the embolus. Other animals which were immunized intratracheally with the same amounts of vaccine and which had had a rest period of the same length as the animals in the groups just mentioned were killed with their normal controls on the fifteenth, twentieth, twenty-fifth and thirtieth days following embolization to permit study of the rate of healing at later periods. All of the animals were killed by electrocution, as in the previous groups, and their lungs were studied grossly and microscopically.

In the normal animals, one day after embolization, the embolus was still within the pulmonary artery, the wall of which was edematous and infiltrated with polymorphonuclear leukocytes. The surrounding pulmonary tissue was edematous, containing many red blood cells closely packed into the contiguous alveoli. Immediately about the artery a zone of polymorphonuclear leukocytes was forming, and the alveolar walls, when they were preserved, were thickened by a swelling of the septal cells. At two days, the wall of the artery was necrotic or ruptured, and polymorphonuclear leukocytes were streaming in toward the embolus through breaks in the wall. After the third day, many large macrophages began to appear in the area about the embolus, and when the embolus had lodged near a large bronchus the tendency toward a fibroblastic response was rather marked. From this time to the tenth day, the process was one of an advancing infection, with the zone about the embolus showing evidences of softening and early cavity formation, with little tendency toward an active organization of the inflammatory exudate before the ninth day.

In the immunized animals the reaction during the first four days was characterized by a larger zone of hemorrhage about the site of the embolus; as a result, the embolus was much easier to locate in the immunized than in the normal animals. When the hemorrhagic areas in the immunized animals were incised, the edema was always more intense than in the normal animals. In the later periods (from five to nine days) the zone of cellular infiltration about the embolus was grayish yellow and firmer than in the normal dogs.

Microscopically, the zone of hemorrhage and edema about the embolus in the immunized animals was conspicuous, and the greater number of swollen septal cells and large foamy macrophages in the exudate around the embolus was readily apparent. The polymorphonuclear leukocytes appeared to be much better preserved, whereas in the normal animals leukocytic fragmentation and cellular degeneration were generally present and at times marked. Fibroblasts became increasingly numerous after the fifth day.

Surprisingly, the large numbers of red blood cells within the alveoli, so prominent a feature of the early periods, had almost disappeared in both the normal and the immunized animals killed on the seventh and the ninth day.

Observations on the animals killed after ten days revealed a continuation of the process seen in the early periods. In general, in the immune animals killed on the twentieth and the twenty-fifth day the embolus was found to be surrounded by a rather dense wall of fibroblasts, while in the normal animals active inflammation was evidenced by many polymorphonuclear leukocytes, small cavities and a fibroblastic ingrowth less abundant than that seen in the immune animals.

It may be said, then, that the response of the lungs of immune animals in the early period, in which the reaction was exudative, and in the later period, in which it was primarily a reaction of healing, was always more marked than that in the lungs of untreated animals.

COMMENT

The theoretical bases underlying these experiments justify detailed analysis, as the facts tend to substantiate further the validity of the original assumption that differing levels of pulmonary resistance may be secured by appropriate immunologic devices.

The anatomic nature of the pulmonary alveoli, with the intimate relationship of the air to the blood stream, suggests the presence of a barrier permeable to gases and fluids but impermeable to inhaled particles. Figure 10 reveals the mechanism of this barrier in the lung of a dog into which living staphylococci had been introduced through the trachea approximately seventy-five minutes before. The entrapping of the bacteria by the septal cells both while they were attached and while they were detached, associated with the adherence of bacterial particles to the interalveolar reticulum, affords considerable evidence of the manner in which particles are prevented from invading the blood stream.

The further fate of the bacteria is probably closely linked with that of the septal cells. The coughing up and expulsion of these cells should eliminate the bacteria within them, but it is improbable that under ordinary conditions a considerable number of septal cells are disposed of in this way. Their morphologic resemblance to macrophages elsewhere in the body suggests that they may also participate in the formation of

antibodies through their digestion of engulfed bacterial particles. Such locally formed antibodies should therefore permeate the pulmonary tissues as well as diffuse into the lymphatics and the blood stream. The experiments of Cannon and Sullivan [18] indicate that the concentration of locally formed antibodies in tissues may vary considerably, being greatest in the tissues into which the antigen is introduced. Under

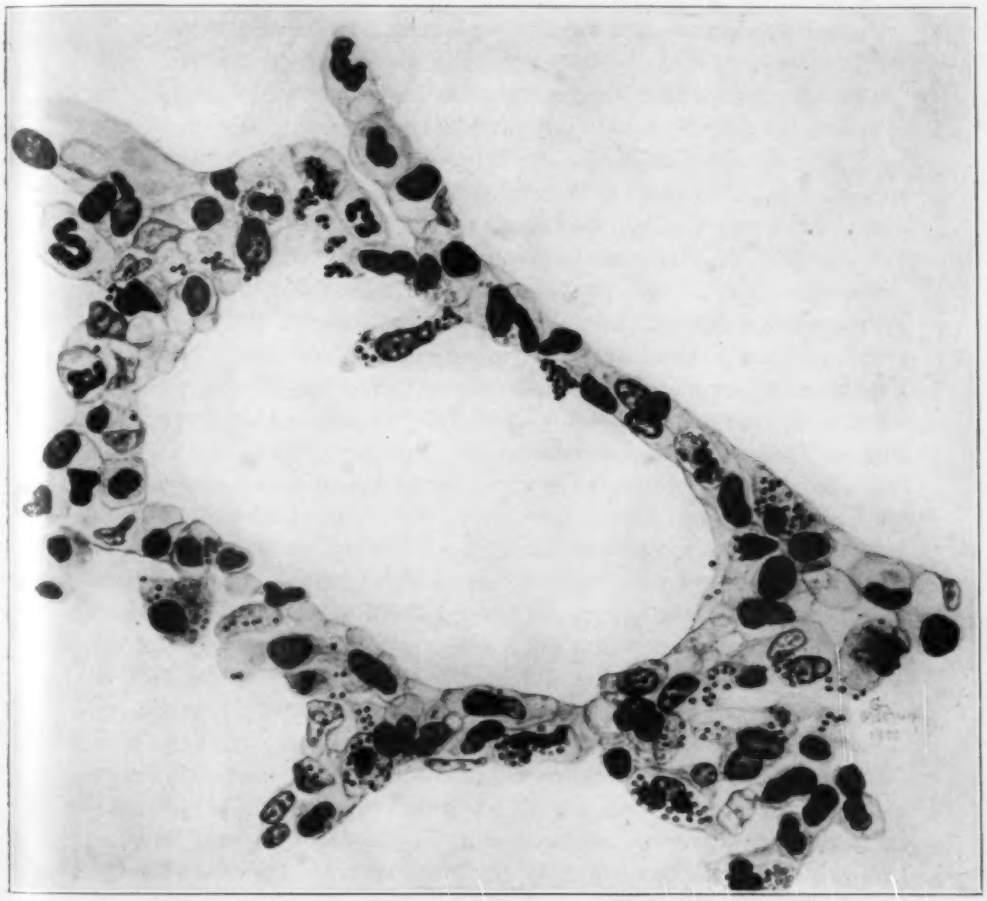

Fig. 10.—Photomicrograph of a drawing made with the aid of a camera lucida of a section from the lung of a normal dog seventy-five minutes after the intratracheal introduction of a suspension of staphylococci. Note the engulfment of the cocci by septal cells and the adherence of clumps of bacteria to the septal wall.

the conditions of our experiments, therefore, a greater concentration of antibodies might be expected in the pulmonary tissues, whence they would tend to diffuse gradually into the blood and lymph streams in

18. Cannon, P. R., and Sullivan, F. L.: Local Formation of Antibody by the Skin, Proc. Soc. Exper. Biol. & Med. **29**:517, 1932.

the process of generalized passive immunization. There is no direct proof, however, that such local formation of antibodies occurs in the lungs, although study of this problem is now in progress. Furthermore, any antigen which passes the primary pulmonary epithelial barrier during the course of intratracheal immunization causes development of a generalized active immunization concomitantly with the development of a local pulmonary immunity.

The introduction of a foreign protein of particulate nature into the lungs stimulates the tissues to cellular proliferation, and the actual increase in the number of immature basophilic mesenchymal cells in an irritated lung of this sort presumably results from such a stimulus. The later differentiation of these cells into functionally mature macrophages, from the direct proliferation of septal cells in the septal wall, from the emigration of monocytes from the blood stream into the alveolar septum or from the proliferation of undifferentiated cells in the adventitia of the blood vessels, provides increased numbers of phagocytic cells for reaction to further injury. This enlarged reservoir of phagocytic cells, therefore, by engulfing antigenic particles and possibly by liberating specific antibodies into the pulmonary structures, should serve to elevate the level of resistance of the lungs to subsequent infection with the homologous living micro-organism.

What is the most probable effect of an increased concentration of antibodies in these tissues? According to Rich,[19] antibodies in tissue increase the adhesion of the homologous bacteria to the tissue and to one another, thus limiting the extent of their "drift" through the tissues. In this way infection remains localized and less serious than if it was the consequence of a generalized dissemination of the bacteria. The experiments of Cannon and Pacheco [20] pointed in the same direction and placed a further emphasis on a more efficient bacteriotropic action in the facilitation of phagocytosis, thus favoring both the immediate and the continued localization of the invading bacteria. In whatever manner the bacteria are fixed, it is obvious that in pulmonary infection the degree of dissemination in the blood stream will vary inversely with the initial ability of the lungs to fix the bacteria effectively and with the facility with which the phagocytic septal cells and polymorphonuclear leukocytes engulf and destroy them.

In our experiments, the lungs are probably at a more marked disadvantage than under conditions of natural infection, for whereas in infection by aspiration the infectious agents come into direct and immediate contact with the pulmonary tissue and cellular barriers, this contact is

19. Rich, A. R.: The Prevention of Spread of Bacteria in the Immune Body, Bull. Johns Hopkins Hosp. **52**:203, 1933.

20. Cannon, P. R., and Pacheco, J. L.: Studies in Tissue-Immunity: Cellular Reactions of the Skin of the Guinea Pig as Influenced by Local Active Immunization, Am. J. Path. **6**:749, 1930.

delayed for twenty-four hours or more when the infection follows embolization of a pulmonary artery. During this period the bacteria may grow within the embolus, protected to a large extent against leukocytic infiltration by the wall of the pulmonary artery. Furthermore, embolic obstruction of the artery should seriously disturb the normal pulmonary architecture because of the resulting circulatory interference. Therefore, locally mobilized phagocytes and a locally increased concentration of antibodies are of little avail, presumably, until the wall of the pulmonary artery has been eroded and direct contact between the bacteria and the defensive elements of the body has been established. Furthermore, chance localization of an infected embolus near the pleural surface or a large bronchus, especially if the condition is complicated by undue coughing, may interfere seriously with defensive reactions which under more favorable conditions would be adequate. Consideration of these adverse possibilities, therefore, makes the sharp contrast in the tissue reactions in these experiments the more remarkable.

The evaluation of the comparative effects of local versus general immunization is also highly important. The possibility of elevating the local pulmonary defenses to the point of practically closing a portal of entry justifies exploration of these local immunizing procedures. Local concentration of antigen within the lungs can best be secured by its intratracheal deposition and retention; this is not possible if the antigen is introduced in any other way, i. e., intravenously or subcutaneously, as most of it passes through the lungs and eventually localizes in the liver and spleen. Thus the principal immunologic benefits to the lungs which occur later come indirectly from the presence of protective antibodies in the blood stream and then in too dilute concentrations to be quickly effective in a local infection of the lung. Theoretically, both local and general immunization are indicated, but prophylactically, local methods deserve greater consideration because of the possibility that these immunized tissues may be better able to meet a threat of infection quickly and effectively.

The problem of specificity also deserves consideration. Our experiments, although few, offer no encouragement to the view that nonspecific immunization is as effective as specific measures in elevating the reacting capacity of the tissues. Specificity is a principle of immunology which has stood the test of time well, and it probably should be given primary consideration whenever it is practically possible to do so.

The presence of antibodies in the lungs of the immunized dogs was not determined directly by serologic procedures, but suggested by the morphologic observations. A surprising feature was the ability of the bacteria to grow in the agar emboli in the immune tissues, in which the colonies formed and grew, not in the depths of the agar farthest away from the possible effects of bactericidal antibodies, but at the edge of the embolus nearest to the tissue fluids (fig. 11). It is obvious,

therefore, that the killing effects of these antibodies were not conspicuous in vivo. No agglutination of bacteria, as described by Cannon and Pacheco in the skin of guinea-pigs locally immunized against staphylococci, was observed. The greater numbers of bacteria within the phagocytes in the immune dogs and their tendency to become packed together until the outlines of the cell bodies were no longer discernible suggest an enhanced bacteriotropic action in the lungs of the locally immunized animals.

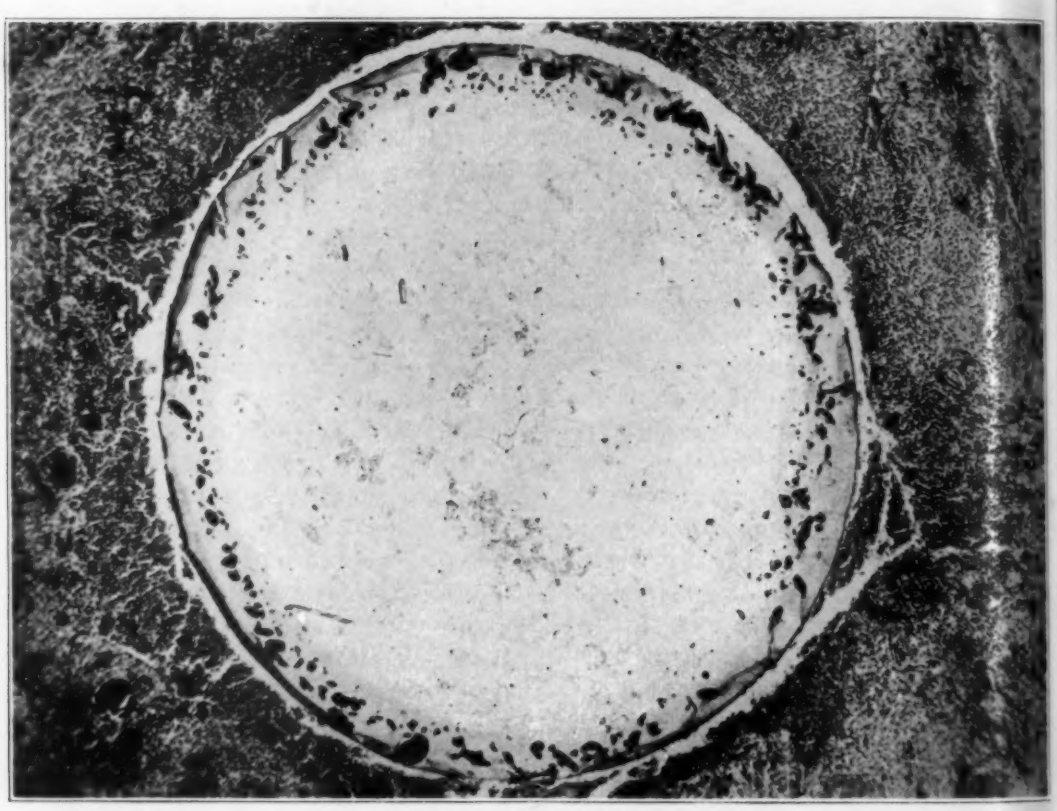

Fig. 11.—Photomicrograph of a cross-section of an agar embolus within a locally immunized lung. Note the bacterial colonies at the periphery of the embolus and their absence in the center; × 36.

The significance of the increased numbers of basophilic mononuclear cells forming "collars" around the blood vessels is probably of more theoretical than practical importance. If our assumption is correct that this indicates a mesenchymal activation by which large reserves of functionally active potential phagocytes become available, it is not so important whether they arise in situ or by migration of monocytes from

the blood stream. The sharpness of the outer edges of the "collars" and the frequency of mitoses, however, incline us to the view that many of these cells arise in situ from the undifferentiated cells of the adventitia of the blood vessels and therefore correspond to the adventitial cells described by Marchand. It should be added, however, that increased numbers of monocytes are present in the lumens of the blood vessels, and that these also are probably leaving the blood stream constantly.

SUMMARY AND CONCLUSIONS

The effects of local, general and nonspecific immunization on the course of development of experimental pulmonary abscess in the dog were determined. Dogs were immunized subcutaneously and intratracheally with vaccines of Staph. aureus or B. coli killed with formaldehyde; later, pulmonary abscesses were produced by the introduction into the external jugular vein of an agar embolus containing living staphylococci or colon bacilli. Ten days later, as a rule, the pulmonary abscesses were examined grossly and microscopically as to the size, the formation of cavities and the state of healing. The general results may be summarized as follows:

1. Abscesses in intratracheally immunized dogs were, in general, smaller, more circumscribed and less subject to the formation of cavities than those in normal or subcutaneously immunized animals.

2. Organization of the inflammatory exudate developed much more rapidly in the intratracheally immunized dogs than in the normal or the subcutaneously immunized dogs.

3. The infecting bacteria remained more localized in intratracheally immunized animals and were engulfed in larger numbers by pulmonary phagocytes.

4. Local pulmonary immunization was superior to general immunization in facilitating the circumscription and healing of the abscesses produced.

5. Specific immunization was more effective than nonspecific immunization in restricting the development and extension of pulmonary abscesses in the dog.

EPITHELIOMA FOLLOWING AVULSION OF THE SCALP

REPORT OF A CASE

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Two types of avulsion of the scalp, complete and incomplete, are generally recognized. Complete avulsion defines those cases in which part or all of the scalp is torn entirely free from its attachments. The incompletely avulsed scalp is left attached to some part of the head by a pedicle.

At present, complete avulsion is almost always exclusively the result of an industrial accident. It occurs chiefly in manufacturing plants where rapidly revolving shafts and wheels are used and more particularly where such moving parts are inadequately housed. The hair becomes caught in the whirling machine, and a sudden force, quickly transmitted, removes the scalp. Because of this mode of occurrence the accident is limited almost entirely to women. Avulsion of the scalp occurs frequently with farm machinery also; a few scalps have been lost by burning; in frontier days scalping by Indians was encountered, and other isolated and bizarre methods have been reported.

Usually the scalp separates in the fatty layer of tissue between the aponeurosis of the occipitofrontalis muscle and the periosteum of the skull, and often the denuded area extends from the eyebrows in front to the occiput posteriorly. Cases have been reported in which all the periosteum was torn away, and it is common to find small localized periosteal defects.

Such an extensive wound is often unassociated with serious immediate complications. Pain, hemorrhage and shock, although sometimes severe, seldom lead to death and are often either mild or absent. In some instances the patient has been unaware of the accident until placing his hands on the denuded head, and it is not uncommon for a patient to walk to the physician's office or to travel a long distance to obtain help.

Later complications often prolong healing and therefore make scalping a dangerous mishap. Infection occurring at the time of the accident may remain limited to the surface of the wound, extend into the bone

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to produce osteomyelitis or penetrate the skull along venous channels to initiate meningitis or abscess of the brain. Hemorrhage and pain, although absent at first, are often troublesome complications later. Exfoliation of the bone usually occurs when there are large periosteal defects. If the wound is allowed to epitheliate spontaneously, formations of scar tissue produce marked retraction deformities. Most serious among the latter is the mild or marked ectropion which may occur in cases in which the line of tearing included the eyebrows or eyelids. Later, ulcers are prone to develop in the newly epitheliated or grafted areas. Many other unusual complications are reported.

In treating patients with complete avulsion, it is useless to replace the avulsed scalp, since it invariably sloughs away. However, early skin grafting in some form prevents later complications from scar tissue retractions. Heterogeneous and even homogeneous skin grafts are unsuccessful, whereas autoplastic grafting gives satisfactory results. Granulations may be secured to cover denuded bone by boring through the outer table of the skull. More specific forms of treatment, outlined by many authors, are beyond the scope of this article.

The mortality from complete avulsion is from 8 to 20 per cent according to various authors. Davis, in a thorough review of cases reported up to 1911, found eight deaths in eighty-five instances of complete scalping. In fifty-three cases reported since that time which I have reviewed the mortality was calculated to be 7.5 per cent. However, the final result was not given in some of the reports.

Incomplete avulsion, in contradistinction to the complete form, is seldom caused by accidents with rotating machinery. Glancing blows on the head, falls, scraping under wheels and other mishaps encountered in the general walks of life account for most cases of this kind.

As might be surmised, the type and extent of the wounds of incomplete avulsion are varied. Occasionally the entire scalp from the eyebrows to the occiput may remain attached only to a pedicle anteriorly or posteriorly, but more frequently the wound is of smaller extent.

When the partially avulsed scalp is sutured into place, healing occurs rapidly if the pedicle by which the denuded flap is attached carries an adequate blood supply. For this reason incomplete scalping is a much less serious accident and is seldom followed by the complications and difficulties seen after complete avulsion.

The following report concerns a fatal case of complete scalping, remarkable for the complications which followed and for their late appearance.

REPORT OF CASE

History.—A. D., a white woman, aged 34, was admitted to Barnes Hospital on Jan. 11, 1928.

No relevant facts were found in either the family or the personal history. Her present illness began in 1907, twenty-one years previous to admission, when, while working in an underwear factory, her hair was caught on a revolving shaft. The scalp was completely avulsed. The two terminal phalanges of a second finger and an entire index finger were torn away at the same time. Profuse bleeding and shock occurred at the time of the accident, but there was no loss of consciousness. The patient stated that there was no fracture of the skull, although she thought the bone was injured. No roentgenograms were made.

Immediately after the accident the avulsed scalp was sutured in place, but it sloughed off in a few days. During the first eleven days of the two months spent in bed, there was high fever. Six months after the casualty, a single unsuccessful attempt was made to graft skin, taken from the thigh of the patient's mother, on the denuded area. Following this operation, the wound was allowed to heal by spontaneous epitheliation, a process which required sixteen years for completion. It was accomplished in 1923.

Meanwhile, in 1918, the patient married. In 1924 she became pregnant and was successfully delivered of a normal girl. Shortly before the birth of the child, a shallow ulcer, about 1½ inches (3.8 cm.) in diameter, formed over the vertex of the skull. There was little discharge from the area, and it was considered of no consequence. Subsequent healing and reappearance of the ulcer occurred, and at times the recurrent ulcerations were associated with a discharge of purulent material. Otherwise the patient was well until the birth of her second child in 1928, six months previous to her admission to the hospital.

Shortly before the delivery of the second child, it was noted that the ulcer formed a "hole" about ¾ inch (1.9 cm.) deep in the top of the head. Dull and constant but rather mild pains occurred in the forehead and temples and sometimes in the face. The pains increased in severity and sharpness and became shooting. At the same time, the purulent discharge increased. On Jan. 11, 1928, the patient came to the outpatient department of Washington University and was admitted to Barnes Hospital.

Physical Examination.—Examination revealed an active, alert woman in no apparent discomfort, with a good memory and no defects of speech. A foul odor was noted.

A wig was worn, and its removal disclosed a large scar covering the top of the head. The margin of the scarred area formed a circle about the calvarium. In front it ran diagonally across the forehead from left to right somewhat below the hair line. Laterally it crossed each temporal region about 2 inches (5 cm.) above the ears, and posteriorly it extended just below the occipital protuberance. On the right side there was an extension of the scar over the zygoma and down onto the cheek. A thin rim of hair remained about the sides and back of the head.

In the middle of the large scar, at the junction of the parietal and occipital bones, was an ulcer measuring 1½ inches in diameter. The margins of the ulcer were composed of granulation tissue which surrounded a base of black, dead-looking bone. In the center of the crater the dura was covered with a small amount of granulation tissue and some pus. At this point the ulcer was about ½ inch (1.2 cm.) deep.

The scar over the right eye had pulled the eyebrow about an inch above its normal position and laterally. The vision in both eyes was good. The right pupil was slightly larger than the left, but both were round and regular in outline and reacted to light and in accommodation. There was no nystagmus, and ophthalmoscopic examination revealed normal eyegrounds.

A careful systemic and neurologic examination disclosed nothing of importance. A diagnosis of osteomyelitis of the skull was made. Surgical solution of chlorinated soda was applied to the wound, and much of the necrotic bone was removed with forceps.

Course.—During the first three months of the patient's stay in the hospital, efforts were made to cause spontaneous healing of the ulcer. Surgical solution of chlorinated soda and petrolatum and mercurochrome dressings were used to combat the infection. Under such treatment the wound improved; in about two months it appeared to be fairly clean but showed no tendency to heal. Microscopic examination of tissue removed from the margin of the ulcer revealed marked proliferation of the epithelium and pearl formation, associated with round cell infiltration. The process was considered to be one of chronic infection rather than one of malignant character.

Because infection persisted and the wound failed to heal, it was decided, three months after the patient's admission, on April 12, to excise the infected area. Bone and soft tissue were removed for 1½ inches about the margin of the ulcer. The patient gradually recovered from the operation, and two months later, on June 16, the wound was considered in condition for grafting. During this time there was occasional headache on the right side which extended down onto the right side of the face.

On June 16 a flap from the left lower portion of the abdomen was attached to the left forearm. On November 21 it was raised and transferred to the head. A week later infection supervened, and the graft was removed from the head and folded on itself on the arm. Attention was again turned to making the wound clean.

Meanwhile, biopsy sections taken from time to time showed marked hyperplasia, apparently due to chronic inflammation.

On Jan. 24, 1929, the patient had a localized convulsion and fainted. On February 10 she fell while going to the bathroom. The following day she grew comatose, with the temperature 40 C. (104 F.) and the pulse rate 140 per minute. Spinal puncture showed a cloudy fluid. Gram-positive organisms were found in a smear from this material, and culture showed hemolytic streptococci. Drainage was established by means of a laminectomy. That evening the patient was moribund. On the following day, February 12, the temperature rose to 41.8 C. (107.2 F.) and the breath was gasping. The heart and respiration failed simultaneously, and the patient died. An autopsy was performed two hours after death.

Autopsy.—On the surface of the body were the scars produced by the plastic operation described. The abdominal flap remained attached to the left arm by a pedicle.

On the head was a large scarred area, the center of which was ulcerated. The outer margins of the scar extended from over the right eye to the occipital protuberance and laterally to about 2 inches above each ear. Thin skin covered only the outer portion of the area, while the center was occupied by a large infected ulcer which measured about 15 cm. in diameter and covered the top of the calvarium. Its somewhat elevated surface was composed of grayish, swollen, foul-smelling granulation tissue. Pus covered some regions. From beneath the ulcer, portions of the frontal, parietal and occipital bones had been removed so that the soft tissues were compressible from the outside.

Brain: The infected granulating ulcer was clipped away and removed with the brain. It was intimately attached to the dura, and over the right cerebral hemisphere it was attached to the substance of the brain itself. The falx cerebri was thickened. A heavy coat of yellow purulent exudate surrounded the base of the brain and extended over the under surfaces of the cerebellum and temporal lobes.

The brain and the attached granulation tissue were hardened in a dilute solution of formaldehyde before cutting. Sections made through the frontal lobes showed the infected ulcer closely adherent to the dura and cortex on the right side. Beneath this area a strip of darkened, softened brain tissue led to the cavity of a large abscess which measured about 4 by 5 cm. and occupied portions of the right frontal and parietal lobes (fig. 1). It was filled with thick purulent material and was lined with rough, dark, necrotic-looking tissue. For some distance about the abscess the brain tissue was softened and discolored, and in one area, where the cavity lay in close relation to the lateral ventricle, extension of the infection into the anterior horn had occurred. The ependymal lining was dull, roughened and covered with a thin layer of exudate. Sections made through the remainder of the brain showed no other lesions.

Fig. 1.—Section of the brain at the level of the abscess. The covering of malignant, infected granulation tissue is shown attached to the upper surface of the right cerebral hemisphere. Necrotic brain tissue extends from this point to the cavity of the abscess. Distortion of the ventricular system is apparent.

Viscera: Examination of the abdominal and thoracic viscera revealed few changes of importance. There were healed tuberculous foci in the upper lobe of the left lung and in the middle lobe of the right lung. The spleen weighed 315 Gm. and was dark red, and the pulp was somewhat softened.

Scalp: Microscopic examination of section 1, taken from the healed border of the scarred area, revealed a connective tissue base over which stratified squamous epithelium had grown. The epithelium appeared to be normal, but toward the edge of the scar it was thinned to a narrow layer, 1 or 2 cells in thickness. Beyond this area were a few islands of epithelial tissue on the surface of the wound. No evidence of malignant transformation was found in this section. The connective tissue beneath the epithelium was rather dense, with an abundance of pink-staining

collagenous material. Many lymphocytes and large mononuclear cells and some plasma cells were found between the connective tissue strands, and the number increased as the margin of epithelization was approached

Section 2 was taken from the center of the ulcer. The outer surface was covered with a pink-staining, amorphous, necrotic exudate mixed with a small amount of fibrin and numerous blue-staining clumps of bacteria. Remnants of epithelial cells were prominent in this layer. In some areas lymphocytes and swollen macrophages were found beneath, as well as in, the layer of necrotic débris, while in other parts dense accumulations of polymorphonuclear cells and bacteria were present, especially at the sites where the tissue, on gross inspection, appeared to be infected.

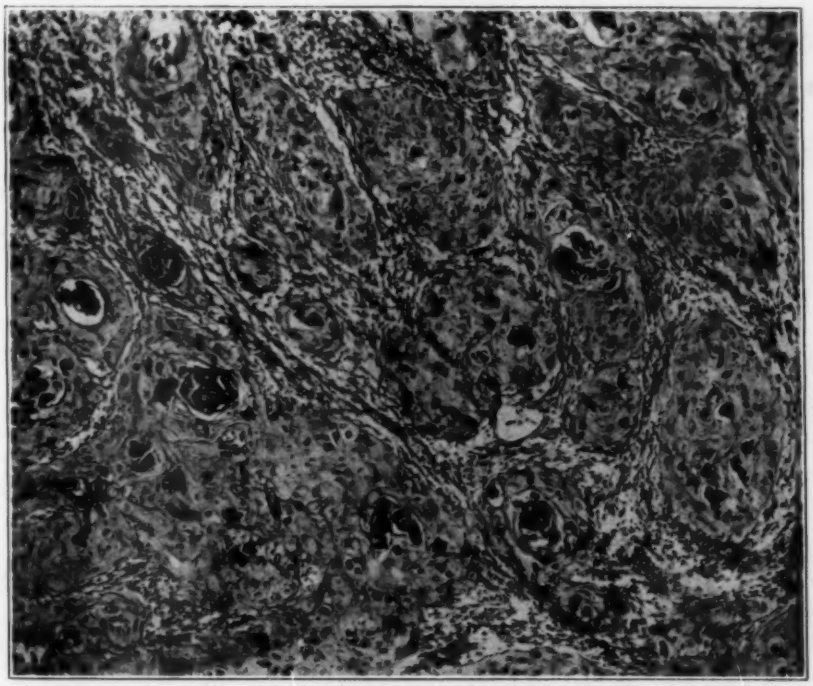

Fig. 2.—This section is *A* in figure 1, from below the ulcerated surface of the scalp. Flat sheets and nests of malignant epithelial cells are shown lying in a loose connective tissue stroma. Lymphocytic infiltration of the stroma is marked.

These more superficial layers merged gradually into the deeper tissue, where there was a malignant proliferation of epithelial cells. An abortive attempt at epithelization was found in some of the cracks and crevices on the surface of the ulcer, but beneath such areas the cells extended directly into the tissues below. Here, in the deeper layers, epithelial tissue had grown in disorderly anastomosing strands, flat sheets, solid masses and isolated islands (fig. 2). The cells were large and swollen, and some were in the process of mitotic division. Where they had become separated from the peripheral blood supply they had invariably degenerated, and appeared as swollen, pink, hyalinized cells with pyknotic or faintly staining nuclei. In the center of epithelial nests, the typical pearl formation of squamous

carcinoma was noted. Some of the keratinized areas were undergoing solution, and many polymorphonuclear and large mononuclear cells were seen in their central parts.

Between the strands of malignant epithelial tissue ran a rather loose connective tissue stroma which was densely infiltrated with lymphocytes and macrophages and a few polymorphonuclear cells.

Brain: Section 1 was taken in order to study the relation of the brain to the infected granulating wound on the surface and the extension of the infection from this site to the abscess of the brain. A portion of the wall of the abscess was included.

The outermost portion of the section thus showed a thin strip of tissue similar to that described as present in the section of the scalp. Beneath this layer was

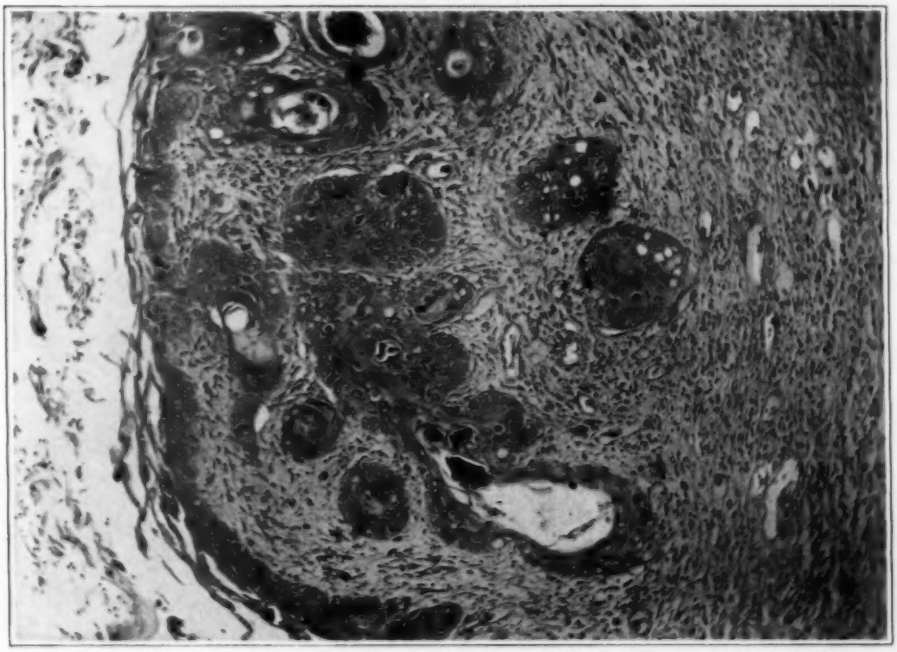

Fig. 3.—This section is *B* in figure 1, a portion of the wall of the abscess of the brain lined with squamous epithelium. Invasion of the brain tissue by malignant cells has occurred beneath this lining.

the region occupied by the meninges. Only remnants of those structures, marked chiefly by blood vessels, remained. In most places, connective tissue and epithelial cells had invaded and obliterated the dura and pia-arachnoid and were in direct contact with the brain. Some epithelial cells had grown for a short distance into the cortex. In other areas dense accumulations of polymorphonuclear leukocytes, with fibrin and much necrotic débris, occupied the region of the subarachnoid space. At such sites the walls of many blood vessels were surrounded and invaded by inflammatory cells. Necrosis and rupture of some vessels, apparently veins, had produced small hemorrhages into the exudate. Blue-staining clumps of bacteria were prominent everywhere.

Beneath the portion just described the brain substance was destroyed almost beyond recognition. Extension of polymorphonuclear cells into the cortex had occurred, especially about numerous dilated blood vessels, but there was also a diffuse infiltration of the intervening tissue. In some areas, collections of these cells and the solution and disappearance of nerve tissue had progressed to the formation of small abscesses. Few living nerve cells were found; in most places the cells had vanished, leaving only neuroglia and large mononuclear phagocytes, while in other regions they contained pyknotic nuclei and shrunken, granular, pink-staining cytoplasm. The path of infection could thus be traced deep into the brain substance, where it became localized about the abscess.

The wall of the abscess was lined irregularly with dense accumulations of polymorphonuclear and large mononuclear cells, the cytoplasm of the latter being distended by ingested material. Broken remnants of neuroglia were observed between these cells, and blood vessels persisted far out into the necrotic wall. Some of the blood channels were completely destroyed, and their remains appeared as pink, hyalinized structures; others showed beginning invasion of their coats and thrombosed lumens. Occasionally, accumulations of red blood cells and fibrin marked the site of hemorrhage from one of these vessels.

Epithelial cells, similar to those described as occurring on the surface, were found in the abscess cavity. Most of them were necrotic, and their degenerated remains suggested that they had preceded the infection to the site of the abscess. In other places epithelial cells lined the wall of the abscess (fig. 3). Other groups had invaded the brain substance, where in some cases they formed pearls. However, no continuity with the carcinoma cells on the surface could be established in this section.

The destruction of the nerve tissue extended for some distance about the wall of the abscess and many active mononuclear phagocytes had wandered into these areas. Still farther away, small localized hemorrhages had occurred, and occasionally groups of polymorphonuclear cells were found.

Section 2 was taken in order to study the extension of infection from the abscess toward the lateral ventricle. At one point there were necrosis and solution of the ventricular lining with the extension of an exudate of polymorphonuclear leukocytes into the ventricular cavity. The relation of this invasion to the abscess could not be clearly demonstrated at this level.

COMMENT

The late onset of fatal complications and their character make this case unusual. Osteomyelitis, meningitis and abscess of the brain have all been reported following avulsion of the scalp, but they are usually coincident with the acute infection which often immediately follows the accident. That they may result indirectly from scalping twenty-one years after its occurrence is interesting. Such a fact suggests that cases in which the patient is reported as recovered when epitheliation is complete may later show complications. Thus complete avulsion of the scalp may be an even more formidable accident than the records of cases indicate.

The development of an epithelioma in tissue first stimulated to proliferation by a large surface defect and later by infection is interesting but not unusual. It is well known that any chronic ulcer may

become the seat of a cancer (Graham) and that many forms of physical and chemical irritation may produce epithelioma of the skin (Ewing). Loeb, in discussing the etiology of cancer of the skin divided the irritating agents into two groups, internal and external. While both factors are present in the majority of cases, as a rule one or the other predominates. In certain cases only internal factors and in others only external factors are noticeable. Thus in cases of xeroderma pigmentosum some internal factor makes the skin peculiarly susceptible to the action of ultraviolet rays, while the development of cancer from exposure to roentgen rays seems to depend almost entirely on external stimulation. In the case reported here the external irritating agencies played the most important rôle in producing a malignant tumor.

It is not uncommon, of course, for an abscess of the brain to result from the extension of a surface infection along venous channels. In this case, however, at the time of autopsy, direct growth of tumor cells across the meninges and through the brain substance was established. From the histologic study it seems probable that these cells preceded and marked the path of infection which developed later.

SUMMARY

A case of complete avulsion of the scalp is reported in which the sequence of events was as follows: (1) spontaneous epitheliation over a period of sixteen years; (2) subsequent ulceration and infection of a portion of the healed area during pregnancy; (3) development of osteomyelitis of the skull, which later necessitated removal of the top of the calvarium: (4) failure in attempts at plastic repair, and (5) death with symptoms of meningitis twenty-one years after the accident.

Autopsy revealed: (1) an epithelioma growing in the infected granulating wound of the scalp and invading the brain substance, the development of which was evidently due to the long continued overstimulation of the actively regenerating epithelium contained in the ulcer; (2) an abscess of the brain partially filled with carcinoma cells, communicating with an infected area of the surface and at one point ruptured into the right lateral ventricle, and (3) acute meningitis.

Dr. H. A. McCordock made the photomicrographs.

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GASTRIC SECRETION

VI. THE ACTION OF PILOCARPINE ON THE SECRETIONS OF A TRANSPLANTED GASTRIC POUCH WITHOUT AUERBACH'S PLEXUS

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Although there is no doubt that nervous stimuli excite gastric secretion, the precise source of the autonomic nerves which reach the secreting cells is as yet unknown. Two methods have been available for study: (1) histologic examination and (2) the use of drugs that stimulate and inhibit the sympathetic and parasympathetic systems. Utilizing transplanted subcutaneous gastric pouches previously described,[1] it seemed likely that these might yield results with the appropriate drugs. The pouches were constructed from the body and fundus of the stomach after stripping away the muscular coats together with the myenteric plexus and consisted of mucous membrane and submucosa. They were transplanted to the subcutaneous tissues of the abdominal wall with the blood supply at first intact. The blood vessels were severed at a subsequent operation. The result was a pouch deprived of vagus and sympathetic nerves and also of the myenteric plexus. Only the submucous plexus remained. Even the nerves accompanying the original gastric blood vessels no longer functioned, for the pouches were dependent on the abdominal wall for their new blood supply. The effect of atropine on such pouches has already been reported.

RELATIONS OF THE AUTONOMIC NERVOUS SYSTEM

The efferent pathways of both autonomic systems are believed to consist of two parts. In the case of the sympathetic system, the first neuron arises in the thoracicolumbar segment and passes to one of the paravertebral ganglions or to one of the larger plexuses, such as the celiac plexus. From these ganglions the second or postganglionic neuron passes directly to the distal cells—the muscle cells in the circular or longitudinal coat of the stomach and intestine. The fibers, therefore (according to the present belief), pass directly through the myenteric and submucous plexuses. In the case of the parasympathetic system, the

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† Dr. Klein died on Oct. 2, 1932.

From the Service of Dr. A. A. Berg and the Department of Laboratories, Mount Sinai Hospital.

1. Klein, Eugene, and Arnheim, Ernest: Gastric Secretion: I. A Transplanted Subcutaneous Gastric Pouch, Arch. Surg. **25**:433 (Sept.) 1932.

first neuron arises in the bulbar (vagus) or sacral part of the spinal cord. It is supposed then to pass directly to ganglions situated in the walls of the peripheral structures, e. g., the myenteric plexus. From these ganglions the postganglionic fibers pass to the distal cells.

According to this theory the vagus nerve must communicate with its postganglionic neuron either in the myenteric or in the submucous plexus. The myenteric plexus consists chiefly of preganglionic vagus fibers. Its functions are incompletely understood, but it appears to be concerned with the normal muscular contractions (such as progressive peristalsis) of the stomach and intestine.

Little is known concerning the submucous plexus. It seems to have some relation to the muscularis mucosae. Any sympathetic fibers to this muscle or to the secreting cells may of course pass through it. But the nature of the cells in it and their relations to the vagus system, if any, are unknown.

Where the postganglionic vagus fibers to the secretory cells arise is also unknown. In the transplanted pouches used in these experiments, only the submucous plexus remained, so that the number of possible sites for the action of drugs became more limited.

ACTION OF PILOCARPINE

The present studies were performed with pilocarpine. This drug stimulates the parasympathetic system. It acts, according to Anderson,[2] on the neurocellular junction substance, just distal to the nerve endings. This observation was made on the muscles of the pupil of the eye. After degenerative section of the postganglionic fibers (short ciliary nerves) pilocarpine still caused contractions. Its action was counteracted by atropine. Admirable, however, as these experiments were, further corroboration in other organs seems necessary. Thus, Magnus [3] made some observations on strips of intestinal muscle peeled away from the myenteric plexus which show that pilocarpine increases their tone. This action too is inhibited by atropine. However, the usual marked contractions caused by pilocarpine do not occur in the absence of the myenteric plexus. Whether this is due to the fact that pilocarpine also acts on the plexus or that the removal of the plexus is in itself sufficient to prevent the normal contractions cannot be said.

While, therefore, Anderson's work seems to show that the site of maximum action is at the neurocellular junction, the possibility of some stimulation in the plexuses and the cells cannot be dismissed.

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2. Anderson, quoted by Sollmann, Torald: A Manual of Pharmacology, ed. 3, Philadelphia, W. B. Saunders Company, 1926.

3. Magnus, quoted by Sollmann.[2]

As regards previous experiments, Suda studied the effect of pilocarpine in a Bickel pouch.[4] The latter is a gastric pouch entirely severed from the stomach, but retaining the original gastric blood supply. An attempt is made to section all the nerves visible in the mesentery. Though such a pouch is deprived of the major portion of its nerve supply, it cannot be stated definitely that all the sympathetic nerves in close relation to the blood vessels are severed. And it is also possible that some branches of the vagus nerve which pass through the semilunar ganglion and accompany the sympathetic nerves are missed. However, Suda found that the gastric cells in these pouches secreted acid on stimulation with pilocarpine. Because of the assumption that the branches of the vagus nerve pass directly to the secretory cells and that section of these branches to the pouch has been followed by degeneration of the nerve endings in the secretory cells, Bickel [4] concluded that the drug acts on the substance of the neurocellular junction. But his primary assumption is contrary to the conception now prevelant.

EXPERIMENTS

Tests with pilocarpine were performed on six dogs. Three had the type of transplanted pouch just described. One dog had the same type of transplanted pouch, but the original gastric blood vessels were left intact. Some sympathetic nerves may have reached the pouch along these vessels. The blood supply of this pouch was, however, much better than that of the pouches dependent on the abdominal wall, and the quantity of secretion was greater. This pouch, like the others, consisted only of mucous membrane and submucosa. The myenteric plexus was eliminated. Two dogs with ordinary Pavlov pouches were utilized for comparison.

The doses employed were 3.5, 5 and 7 mg. of pilocarpine hydrochloride. The drug was injected subcutaneously. The inhibitory effect of atropine on the action of pilocarpine was also studied. As in the results reported in previous papers, free hydrochloric acid, total acid and total chlorides are reported in the usual clinical units, that is, in cubic centimeters of decinormal solution. Pepsin is reported in units obtained by squaring the millimeter of Mett tubes digested and multiplying by 16; such results are, of course, not quantitatively accurate, but the relative observations are of some value. Frequently the amount of secretion was so small that determinations on the secretion of pepsin could not be made. In each table the secretion following the administration of 200 Gm. of meat and 250 cc. of water is given for comparative purposes. Altogether, forty-six tests were made. Tables 1 and 2 show the results with each type of pouch.

RESULTS

After doses of 3.5 and 5 mg. of pilocarpine hydrochloride injected subcutaneously, the appearance of free hydrochloric acid was inconstant. After doses of 7 mg. free hydrochloric acid always appeared

4. Bickel, Adolph: Ueber die Pathologie und Therapie der Sekretionsstörungen des Magens, Jena, Gustav Fischer, 1907.

(tables 1 and 2). This was true in all the pouches. Though pilocarpine was not as powerful a stimulant of free acid as histamine, in the larger doses fairly concentrated solutions were produced, the highest

TABLE 1.—*Effect of Pilocarpine Hydrochloride on Transplanted Denervated Gastric Pouch Without Myenteric Plexus*

Hour	Quantity of Juice, Cc.	Free Hydrochloric Acid	Total Acid	Pepsin*	Total Chlorides†
Test with Meat and Water					
1. Fed 200 Gm. of meat and 250 cc. of water	1.2	0	25	16	...
2.	0.7	5	50	..	...
3.	0.3	10	50	81	...
4.	0.55	30	70	..	...
5.	0.82	30	75	..	...
6.	0.64	15	60	64	...
Effect of 5 Mg. of Pilocarpine					
1. 5 mg. of pilocarpine injected subcutaneously	0.6	0	20	..	...
2.	1.4	0	60	64	...
3.	1.3	0	50	100	...
4.	0.7	0	40	81	...
5.	0.85	0	60	..	...
6.	0.60	0	50	..	...
Inhibitory Action of 1 Mg. of Atropine on Effect of 5 Mg. of Pilocarpine					
1. 1 mg. of atropine injected subcutaneously; 5 mg. of pilocarpine injected fifteen minutes later	0.65	..	25	36	...
2.	1.1	0	40	64	...
3.	0.8	..	30	..	...
4.	1.1	..	40	85	...
5.	1.6	0	35	..	...
6.	1.3	0	35	81	...
Effect of 7 Mg. of Pilocarpine					
1. 7 mg. of pilocarpine injected subcutaneously	1.0	0	55	16	...
2.	0.8	55	80	78	...
3.	0.65	0	45	..	...
4.	0.5	0	40	85	...
5.	0.4	0	40	..	...
6.	0.8	0	45	..	...
Inhibitory Action of 1 Mg. of Atropine on Effect of 7 Mg. of Pilocarpine					
1. 1 mg. of atropine injected subcutaneously; 7 mg. of pilocarpine injected fifteen minutes later	1.4	0	10	..	144
2.	0.6	0	15	..	144
3.	0.55	0	15	..	...
4.	0.4	0	15	..	...
5.	0.5	0	10	..	148
6.	0.2	0	10	..	...

* Pepsin is expressed in Mett units.
† Total chlorides are expressed in cubic centimeters of tenth-normal solution.

free acid and total acid encountered being 60 and 115. This action persisted in the transplanted pouches for a period of one year.

After the smaller doses, when free hydrochloric acid was absent, an increase of secretion of pepsin occurred (table 1). The primary effect

apparently is the stimulation of secretion of pepsin and, in larger doses, of hydrochloric acid. This is in conformity with the results of Babkin's investigations.[5]

Owing to the small quantity of the secretion in the transplanted pouches, definite conclusions as to the effect of stimulation on the quan-

TABLE 2.—*Effect of Pilocarpine Hydrochloride on Subcutaneous Gastric Pouch Without Myenteric Plexus but with Original Gastric Blood Supply*

Hour	Quantity of Juice, Cc.	Free Hydrochloric Acid	Total Acid	Pepsin*	Total Chlorides†
Test with Meat and Water					
1. Fed 200 Gm. of meat and 250 cc. of water	0.4	15	55	..	...
2.	7.9	95	130	82	152
3.	3.3	85	115	64	146
4.	3.7	60	95	64	146
5.	3.1	45	90	78	148
6.	2.4	50	100	78	146
Effect of 5 Mg. of Pilocarpine					
1. 5 mg. of pilocarpine injected subcutaneously	0.2	20	45	..	...
2.	5.5	55	115	100	...
3.	2.1	5	60	100	...
4.	2.3	0	75	144	...
5.	0.45	0	60	..	144
6.	0.4	0	25	..	...
Effect of 7 Mg. of Pilocarpine					
1. 7 mg. of pilocarpine injected subcutaneously	0.4	0	50	..	...
2.	3.7	45	85	100	148
3.	1.6	40	75	100	...
4.	0.9	0	55	..	...
5.	0.15	0	40	..	...
6.	1 drop	0	..	..	...
Inhibitory Action of 1 Mg. of Atropine on Effect of 7 Mg. of Pilocarpine					
1. 1 mg. of atropine injected subcutaneously; 7 mg. of pilocarpine injected subcutaneously fifteen minutes later	1.1	0	20	..	...
2.	0.7	0	25	..	144
3.	0.25	0	15	..	...
4.	0.45	0	15	..	...
5.	0.30	0	10	..	...
6.	1 drop	0	..	..	...

* Pepsin is expressed in Mett units.
† Total chlorides are expressed in cubic centimeters of tenth-normal solution.

tity cannot be drawn. Usually, but not invariably, when free acid was present the quantity was increased. In the transplanted pouch with the intact blood supply and in the Pavlov pouches, the quantity was always increased (tables 1 and 2).

One milligram of atropine always inhibited the secretion of free hydrochloric acid produced by 7 mg. of pilocarpine hydrochloride (tables

5. Babkin, B. P.: Die äussere Sekretion der Verdauungsdrüsen, Berlin, Julius Springer, 1928, p. 191.

1 and 2). The quantities of the secretion were also inhibited. When sufficient secretion for a test was obtained, though no free acid was demonstrated, secretion of pepsin persisted (tables 1 and 2).

CONCLUSIONS

It is evident that when allowance is made for the fact that the secretion in the transplanted pouches is much smaller than in the Pavlov pouches, the response in all the pouches to the stimulation of pilocarpine is similar. It is evident too that pilocarpine can stimulate the gastric cells to secrete pepsin and hydrochloric acid in the absence of both vagus and splanchnic nerves.

It is a striking fact that atropine inhibits the secretion of the hydrochloric acid but not of the pepsin produced by stimulation by pilocarpine. They are, of course, secreted by different cells. The variation may be due to the fact that the nature of the secretory process is different in each type of cell. The peptic cells build up "granules" which are then discharged, while the acid cells convert other chlorides to hydrochloric acid.

As the action of pilocarpine persists after the removal of the myenteric plexus, it is effective in the absence of postganglionic vagus fibers arising from the plexus. The possible sites of action that remain are: (1) possible nerve endings of fibers originating in the submucous plexus; (2) the neurocellular junctions, and (3) the cells.

The obvious next steps are the repetition of these experiments with physostigmine and choline.

It is important to emphasize once more that a parasympathicomimetic drug can stimulate gastric secretion in the absence of all extrinsic nerves and of the myenteric plexus. It is desirable to accumulate as many facts as possible tending to show such action in the complete absence of parasympathetic nerve supply. Should this be established it might permit the assumption of a working hypothesis that a stimulating substance may, under normal or pathologic conditions, exist in the peripheral circulation. The presence of such a stimulant would explain many obscure phenomena. In the sympathetic system such a known substance of course exists in epinephine, which maintains its action after all the nerve supply has been eliminated.

SUMMARY

The site of origin of the postganglionic vagus fibers to the secretory cells is unknown. According to present theories, however, this should be either in the submucous or in the myenteric plexus.

Transplanted subcutaneous gastric pouches deprived of the vagus and sympathetic nerves and the myenteric plexus were used for this study. Control studies were done on Pavlov pouches.

Pilocarpine, a stimulant of the vagus system, was the first drug used. It is believed to act chiefly on the neurocellular junction.

Pilocarpine hydrochloride in doses of 3.5 and 5 mg. occasionally stimulates the secretion of free acid and at other times does not. Seven milligrams always stimulates such secretion. The secretion of fluids seems to run parallel to the secretion of acid. While the amount and the concentration of acid are not as high as after the injection of histamine, appreciable levels may be reached. The highest encountered in these experiments was 55 free acid and 115 total acid. This action has persisted for one year after the preparation of the pouch.

The smaller doses stimulated the secretion of pepsin even when no free hydrochloric acid appeared.

Atropine in doses of 1 mg. always inhibits the secretion of free hydrochloric acid and of fluid produced by full doses of pilocarpine hydrochloride (7 mg.). This is contrary to its effect on the action of histamine, which, with adequate doses, cannot be inhibited.

Atropine does not inhibit the secretion of pepsin produced by the injection of pilocarpine.

Pilocarpine remains effective after the vagus and the sympathetic nerves and Auerbach's plexus are eliminated. The exclusion of the plexus signifies the elimination of any postganglionic vagus fibers and their nerve endings which may originate there.

Experiments with choline and physostigmine, which act on nerve endings, should furnish further clarifying data.

TREATMENT OF FRACTURES OF VERTEBRAL BODIES UNCOMPLICATED BY LESIONS OF THE CORD

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Recent fractures of vertebral bodies, uncomplicated by lesions of the cord, can be made to respond to treatment on the same general principles, and as satisfactorily, as major fractures of the large weight-bearing bones. Each of the latter presents distinct problems, owing to fundamental differences in structure and function. This is also true of the vertebral column, largely because of the peculiar structure and functions of the intervertebral disks, the frequent destruction of the disks as a result of injury and the high degree of adaptability of the column to such destruction under favorable treatment.

This thesis represents a study of the clinical course and early destiny of recent fractures of vertebral bodies without injury of the cord, the mechanics of their reduction by hyperextension and the mechanism of possible injury to the cord during reduction. It is based on a study of thirty-one consecutive [1] cases occurring in and near Boston between 1928 and 1932, inclusive.

DIAGNOSIS

Early diagnosis is essential to satisfactory decompression, and accurate diagnosis, to safety in reduction and rational postreduction care. Failure to obtain decompression has occurred when there was a delay of more than seventeen days in making the diagnosis. Postponement of corrective treatment for four or five days or even a week does not seem to jeopardize the patient's chance of obtaining decompression, and occasionally seems wise because of shock, ileus or complicating injuries. But reductions after a week become, in the main, increasingly difficult as time passes. Furthermore, early diagnosis is important from the standpoint of the patient's morale. In a surprisingly large number of cases (13 per cent of the cases concerned here) recumbency was not insisted on by the surgeon in charge, under the impression that the patient had sustained a strain. Patients who are ambulatory immediately following fracture, with mild or no support, frequently experi-

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This paper was presented as a thesis in application for membership in the American Orthopaedic Association.

This study, started in 1926, was made possible by an assignment of cases in the fracture service of the Massachusetts General Hospital.

1. Two cases in which the patients were treated by former methods cannot be traced and are not included.

ence severe incapacitating pain, and thereby come to regard their injury in a light far more disquieting than it deserves when its true nature is finally disclosed. Commonly, the layman believes that fracture of the spine means crippledom, paralysis or death. If the person with an injured spine were rendered comfortable from the start, especially in industrial and automobile accidents, much of this misapprehension could be allayed and better cooperation obtained.

Both from the standpoint of the patient's safety from injury to the cord during reduction and from that of loss of correction during recovery, accurate diagnosis must be obtained. This is possible only through roentgenograms revealing the best obtainable bone detail in anteroposterior and lateral planes. The roentgenograms should include the entire vertebral column, since scattered fractures may be present, some of them silent. The roentgen study should also include the lumbosacral junction for local factors predisposing to subsequent strains, since this region suffers most through failure of correction.

Injury of the spinal cord is in most cases the result of dislocation, either momentary or fixed. Therefore, if dislocation is present, or there is evidence that momentary dislocation occurred at the time of injury, it becomes apparent that the safety of the cord in that case is diminished, and the utmost caution is necessary in effecting reduction or, indeed, proceeding with any policy of treatment.

Patients not showing paralysis but revealing mild symptoms of injury of the cord in the form of reflex changes, bladder retention, paralysis, variations in muscle tone or hyperpyrexia possess a low factor of cord safety. These points should be carefully determined before proceeding with reduction rather than after disaster.

In arriving at an accurate roentgenologic diagnosis,[2] the following points should be carefully noted:

1. (*a*) Loss of the concavity of the anterior surface of the vertebral body; (*b*) zone of increased density; (*c*) intestinal gas patterns suggesting ileus
2. Lateral and anterior wedging
3. Fragmentation and saucerization of the articular surfaces
4. (*a*) Narrowing of the adjacent intervertebral spaces; (*b*) narrowing of the other intervertebral spaces
5. The condition of the posterior bony structures, i. e., the spinous and articular processes, the laminae and pedicles
6. Crushing of the posterior wall of the body
7. Anterior and lateral dislocation of one body on another
8. Spurring (proliferative changes)
9. Defects in the lumbosacral region

2. Dr. William Martin of the department of radiology, Massachusetts General Hospital, painstakingly reviewed all the roentgenograms in this series.

Points 1*a* and 1*b* were present in all the cases and seemed diagnostic; point 1*c* was frequent in very recent cases; point 2 gives an estimate of the derangement of the mechanics of the back and is important from the standpoint of fixation; points 3 and 4 indicate the degree of disorganization of the intervertebral disk; points 5, 6 and 7 give an estimate of the factor of cord safety from the standpoint of reduction, and points 8 and 9 are important in prognosis and indicate a back already predisposed to strain.

Complicating injuries must not be overlooked. Not uncommonly, the os calcis, the sacro-iliac joints, the transverse processes, the ribs and the sternum share with the vertebral body the effect of the trauma.

ETIOLOGY

The usual injuries causing fractures of vertebral bodies and their importance in diagnosis have been frequently and well described in the literature. Attention has often been called to the common error among surgeons of failing to recognize the condition early.

EARLY DIFFICULTIES IN CORRECTING VERTEBRAL INJURIES

Correction of a deformity resulting from compression of a vertebral body was first demonstrated by Dr. Arthur G. Davis of Erie, Pa., in 1924. He fully described his technic in 1929.[3] Prior to the publication of Davis' work, Dunlop of Pasadena, Calif., and I at the Massachusetts General Hospital, working independently, were consistently obtaining corrections—likewise by extension but by widely different technics. Complete hyperextension of the vertebral column is the keynote of reduction by whatever method is employed. Earlier attempts to reduce such fractures were made, some of them forcible, but none was apparently demonstrated to be successful and none of the methods was consistently practiced. The fear of injuring the cord during reduction seems to have been the reason for the failure to carry extension far enough to be successful.

Reports of other methods of reduction rapidly appeared in the literature [4] following the publication of Dr. Davis' article. Full descriptions of these technics, each yielding satisfactory reductions, are given in these articles.

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3. Davis, A. G.: J. Bone & Joint Surg. **11**:133 (Jan.) 1929.

4. (*a*) Dunlop, J., and Parker, C. H.: Correction of Compound Fractures of Vertebrae, J. A. M. A. **94**:89 (Jan. 11) 1930. (*b*) Rogers, W. A.: Surg., Gynec. & Obst. **50**:101 (Jan.) 1930. (*c*) Jones, R. W.: Brit. M. J. **1**:300 (Feb. 2) 1931. (*d*) Dunlop, J., and Parker, C. H.: Radiology **17**:228 (Aug.) 1931. (*e*) Dunlop, J., and Parker, C. H.: J. Bone & Joint Surg. **15**:153 (Jan.) 1933.

The results of treatment in cases of unreduced fracture often leave much to be desired. Studies of the end-results by a number of authors indicate a long period of disability in a high percentage of cases. The cause of disability is usually backache due to muscle strain, not at the site of fracture but along the course or at the attachments of the erectores spinae. Frequently recurring strains are common during the first two years. This is occasioned by the exaggeration of the anteroposterior spinal curves incident to the deformity of a vertebra, and the difficulty which the muscles experience in accommodating themselves to this change. Treatment by postural exercises and support, granted cooperation by the patient, has proved successful, but often at the cost of two years' disability. Spinal fusion has also been tried extensively in uncorrected cases. Fusion in such cases eliminates pain at the site of fracture and in the corresponding peripheral nerve segments (in my experience, very infrequent complaints), but it does not eliminate muscle strain and does not relieve the vertebral column of the decided mechanical disadvantage under which it is placed by the deformity of the vertebra and the common loss of one of its intervertebral disks.

MECHANICS OF REDUCTION

Any analysis of the mechanics of the normal vertebral column must be based at present on the anatomic researches of Schmorl and his co-workers in Dresden, where seven thousand spines obtained at necropsies in the years from 1925 to 1930 have been carefully scrutinized.[5] This extensive material, exhaustively studied, has led to the best scientific description to date of the normal and pathologic anatomy of the vertebral column. This structure may be likened to a flexible segmented rod (Lovett) of great strength, capable of a remarkable degree of adaptation to torsion, tension and pressure and of resistance to mechanical shock and "wear and tear." These properties are possible because of the intervertebral disks, which are essentially highly specialized articulations between the vertebral bodies, and which comprise almost a quarter of the length of the column (Weber). The further functions of protection to the spinal cord, of affording muscle attachments and of posterior reinforcement are provided by the posterior bony structures. The intervertebral disks differ from other articulations in that the tissue of the nucleus pulposus is present, instead of a joint cavity. Whether the nucleus is a fluid confined under pressure within an elastic container, the annulus fibrosus, as suggested by Keyes and Compere,[6] or whether

5. Beadle, O. A.: The Intervertebral Discs, London, His Majesty's Stationery Office, 1931.

6. Keyes, D. C., and Compere, E. L.: J. Bone & Joint Surg. **14**:897 (Oct.) 1932.

it possesses an inherent turgor which is held in check by the elastic fibers of the annulus and the pressure of the vertebral bodies on the intact cartilaginous end-plates, as suggested by Schmorl, the experience of the last five years has convinced me that it must act as the means of contact and hence as the fulcrum between vertebrae. Since the nucleus is not definitely demarcated, and its shape and relative position are altered somewhat with each change in the position of its contiguous vertebrae,

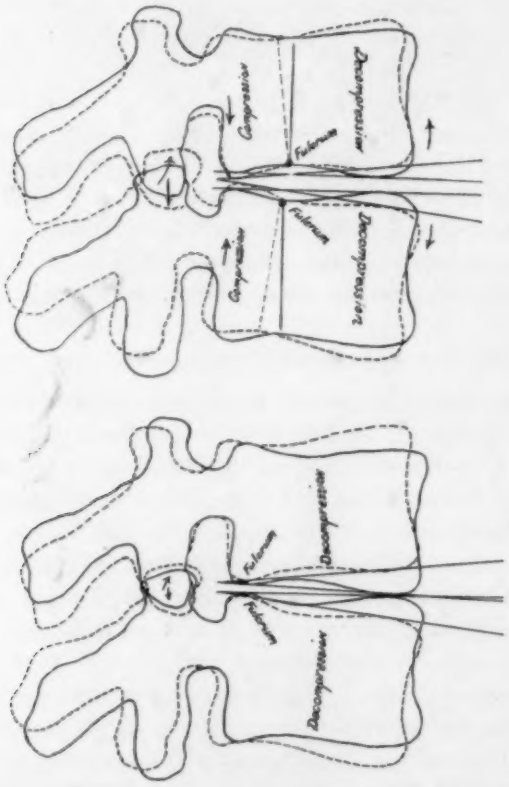

Fig. 1.—Diagram showing mechanics of spinal column: Upper illustration, normal; lower illustration, abnormal as in fracture of vertebra.

this point of contact must shift somewhat with each change in position of the vertebrae. For this reason, it does not seem possible to postulate precisely any single axis of motion between vertebrae. But it may be stated that the axes of motion lie along a line drawn through the point where the greatest resistive pressure of each intervertebral disk falls on its contiguous vertebrae. For all practical purposes, this line falls through the nuclei pulposi (fig. 1 upper part), near the deepest point of concavity of the articular surface of the centrum. Thus, any

force applied to the vertebral column to extend it exerts a decompression or tension throughout those portions of the vertebrae anterior to the line of the nuclei pulposi, and a pressure along those portions of the vertebrae posterior to that line. Along the line there is neither compression nor decompression, and it may be referred to as the neutral line. This may be easily demonstrated by lateral roentgenograms of the lumbar region of a normal person in extreme flexion and hyperextension. The axis of motion of each vertebra may be seen to fall through the concavity opposite the nucleus. It is because of the decompression which occurs in extension that fractures of the vertebrae can be reduced. It may be noted in the roentgenograms in cases in which the disk is not appreciably altered that the vertebra fractured through its superior or inferior surface at or in close proximity to the nucleus pulposus show at that point little or no correction following extension, whereas anteriorly, in the zone of decompression, the centrum may be restored virtually to its prefracture dimensions. Another fractured well posterior or well anterior to the nucleus may be decompressed to such a degree as to represent almost complete anatomic restitution. This consistent finding is interpreted as the result of either a feeble decompression or absence of it in the region of the nucleus, or as the result of a positive pressure from that portion of the disk made up largely of nuclear material.

It was demonstrated by Schmorl's work, and confirmed in the present series, that in injuries resulting in compression fracture the nucleus pulposus is frequently not spared (figs. 2 and 3). It may suffer complete disorganization in severe cases; in others, moderate alteration in which some of its functions may for a time, at least be preserved, or, in some mild compressions, little or no disorganization of either structure or function.

Although the condition of the disk may only be inferred from the roentgenogram, I have divided the cases into four groups for the purpose of analysis of (1) the mechanism of extension and (2) the treatment.

Group 1 includes fractures in which destruction of the disk is slight or absent. Absence of narrowing of the intervertebral space and of evidence of more than minor fragmention of the articular surface seems to indicate that the disk is functioning. The mechanics of extension is virtually that of the normal (fig. 1, upper part). Eight, or 26 per cent of the cases in this series, fell in this group. Excellent reductions were obtained in all (case 1, fig. 4).

Group 2 includes fractures in which the superior or the inferior surface of the centrum and the adjacent intervertebral disk are extensively disorganized. Here it immediately becomes apparent that the inevitable destruction of the nucleus pulposus has deprived the vertebrae of their normal contact and hence normal axis of motion. Extension

occurs through an axis well posterior to the normal—roughly, at the posterior wall of the centrum (fig. 1, lower part). The arc of motion of the laminae and articular processes is short and falls well back of the spinal cord, and the possibility of injury to the cord in extension is almost prohibitive, through the limitation of the longitudinal ligament anteriorly and of the contact and locking of these structures posteriorly. Sixteen cases, or 51 per cent of the series, fell within this group, in all of which corrections were good (case 10, fig. 5; case 12, fig. 6).

Group 3 differs from group 2 only in the deformity of the vertebral body: the compression is essentially central rather than anterior or lateral. The walls of the centrum are but slightly compressed. The

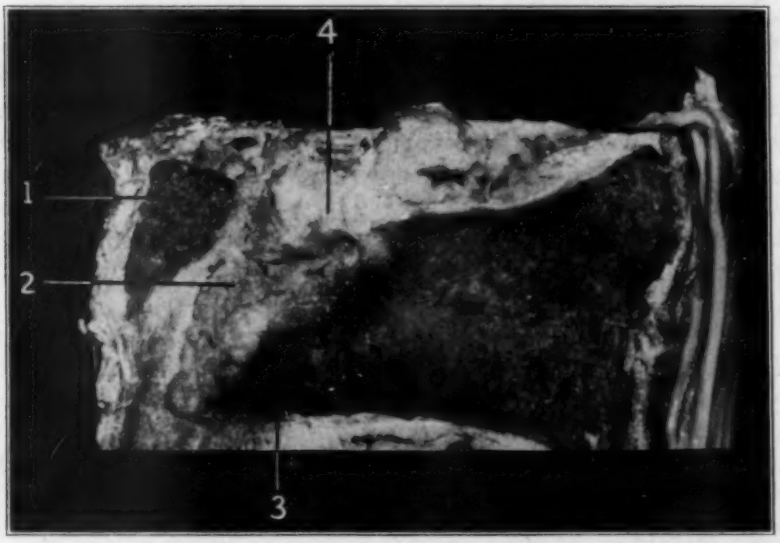

Fig. 2.—Gross photograph of the third lumbar vertebra seven weeks after partial correction. Death occurred from hemorrhage of a gastric ulcer. The vertebra shows: (*1*) anterosuperior bone fragment; (*2*) fracture line (fig. 3); (*3*) hemorrhagic areas and compressed spongiosa, and (*4*) disorganized intervertebral disk pressed into the space between the fragments.

The sections shown in this figure and in figure 3 and the interpretations thereof were made by Dr. Sidney Farber, Department of Pathology, Harvard Medical School.

articular surface is saucer-shaped. Little or no decompression can be obtained by extension. The intervertebral space may be restored. Two cases, or 6 per cent of the series, comprised this group (fig. 7, case 25).

Group 4 includes cases of compression fracture with dislocation of the above adjacent vertebra. The nucleus pulposus has, through the injury, lost its mechanical identity. If during extension posterior replacement of the dislocated vertebra does not occur, the axis of motion falls

through the new point of contact between these vertebrae, namely, near the posterior wall of the displaced vertebra and forward on the superior surface of the fractured vertebra. The arc of motion of the laminae and articular processes of the dislocated vertebra in extension is such that with each increment of extension, these elements encroach farther on the spinal canal until they lock. If, however, the posterior bony proc-

Fig. 3.—Photomicrograph of a section of the specimen shown in figure 2 (× 10; aniline blue stain) taken to include a portion of the anterosuperior fragment, the fracture line and the main fragment. The fracture line contains annular fibers and nuclear material disorganized by the injury and pressed into the fracture mass. The picture shows: (*1*) anterosuperior bone fragment, (*2*) fracture line and (*3*) main fragment.

esses do not lock (always a possibility in fracture of the articular process) injury of the cord ultimately ensues (figs. 8 and 9). Five cases, or 16 per cent of the series, fell in this group.

Fig. 4.—Roentgenograms illustrating injury of vertebra and result of treatment typical of group 1 (case 1). In this case there was no apparent fracture or narrowing of the intervertebral disk. Treatment was by flexible frame, for reduction, and fixation by recumbency in a plaster of paris jacket, ambulatory treatment in a plaster jacket and finally a high backbrace. *A* shows appearance before reduction; *B*, appearance after reduction, during ambulatory treatment in the plaster jacket, and *C*, end-result three years and five months after injury.

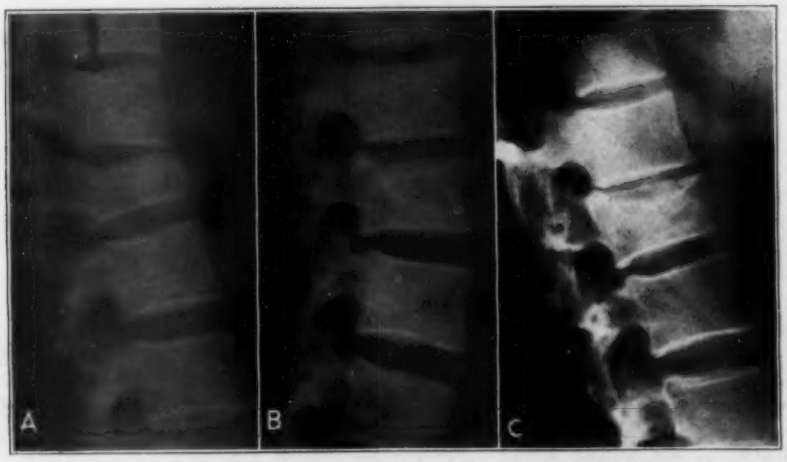

Fig. 5.—Roentgenograms illustrating group 2 (case 10). In this case there was fracture of the superior vertebral surface with no definite narrowing of the intervertebral disk. Treatment was by flexible frame, for reduction, and fixation in shells, followed by fusion and recumbency in a plaster jacket, then by ambulatory jacket treatment and finally a high backbrace. *A* shows appearance before reduction; *B*, appearance after reduction, and *C*, end-result after four years.

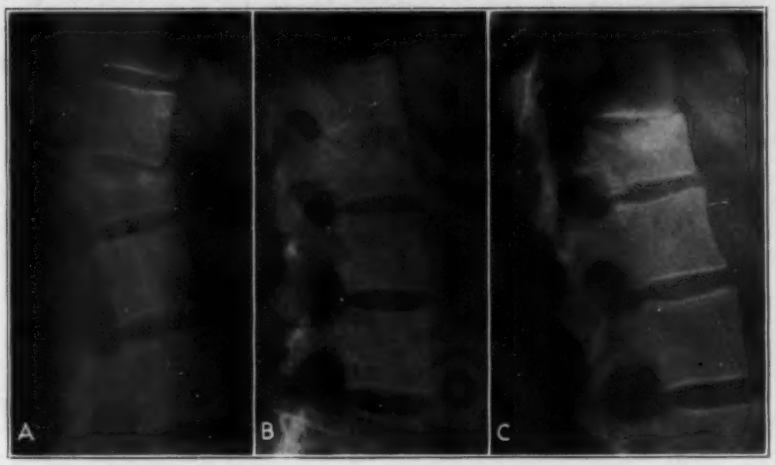

Fig. 6.—Roentgenograms illustrating group 2 (case 12). In this case there was fracture of the superior vertebral surface with narrowing of the intervertebral disk. Treatment was reduction by flexible frame and fixation by shells, followed by ambulatory treatment in a plaster jacket and last a high backbrace. *A* shows appearance before reduction; *B*, appearance after reduction, and *C*, the end-result after four years.

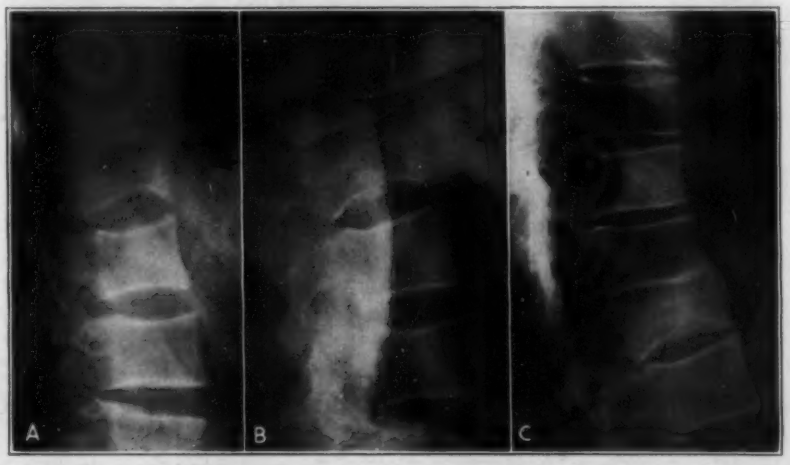

Fig. 7.—Roentgenograms illustrating group 3 (case 25). In this case there were fractures of both surfaces of the vertebra with narrowing of the intervertebral disk. Treatment was reduction by flexible frame and fixation by recumbency in a plaster jacket, followed by ambulatory treatment in a jacket and finally a high backbrace. *A* shows appearance before reduction; *B*, appearance after reduction, and *C*, the end-result after two years and five months.

In one case in this group (case 28) manifestations of impending injury of the cord developed during extension; in another (case 30), so much pain that extension was stopped, apparently just short of injury to the cord, as shown at operation. Posterior replacement of the dislocated vertebrae was obtained in two cases.

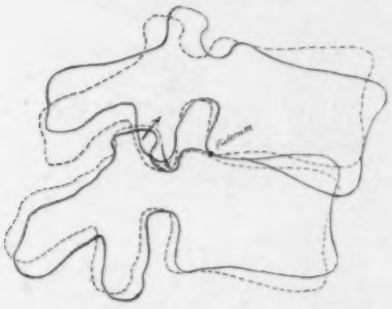

Fig. 8.—Diagram showing mechanics of extension in group 4.

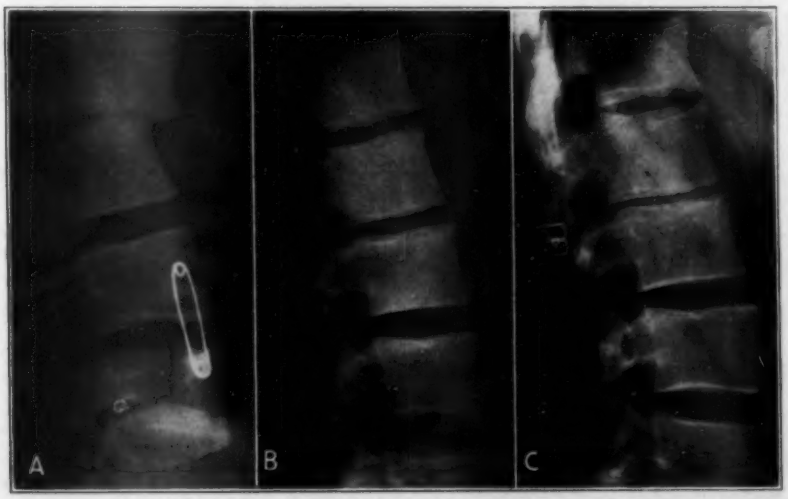

Fig. 9.—Roentgenograms illustrating group 4 (case 27). In this case there were noted: wedging of the vertebral body (anterosuperior lip of second lumbar vertebra), apparent fracture of the anterosuperior lip of this vertebra, obliteration of the intervertebral space, and dislocation of the anterior parts of the first and second lumbar vertebrae. Treatment was reduction by Bradford frames and fixation by shells for three months, spinal fusion, and wearing of a high backbrace. *A* shows appearance before reduction; *B*, appearance after reduction, and *C*, the end-result after four and a half years.

Mention should also be made of the anterior longitudinal ligament which is, as stressed by Davis, so powerful, its tenacity to the vertebral bodies and the disk so great, and its continuity during life so indestructible that it should be mentioned as decidedly a factor in reductions through extension. This ligament limits hyperextension, and with the annulus fibrosus provides the agency through which the forces of decompression operate.

It seems probable that the influences of decompression do not exert their full effect on the fractured vertebrae until complete hyperextension of the intervertebral joints above and below the fracture has been reached, since force applied up to that point is spent in physiologic extension of joints above and below. Clinical experience seems to bear this out. Numerous failures to decompress occurred in cases in which extension was carried out only partially.

APPARATUS AND TECHNIC OF DECOMPRESSION

The apparatus employed in obtaining complete hyperextension in the method of treatment discussed here was described [4b] in 1930 and has remained essentially unchanged since, except that it has been simplified and so arranged that roentgenograms can be obtained at the time of reduction, and plaster fixation applied without moving the patient from the frame. The essential principle of placing the patient supine on a flexible Bradford frame and obtaining extension by rendering the frame convex upward is the same. The flexible frame, in its segment which underlies the vertebral column in extension, assumes virtually the normal extension curve, except in the upper dorsal region where a thickening of the mattress of blankets employed evens the pressure. The force is very great and is under absolute control. It may be applied so gradually that increments of extension are scarcely appreciable by the patient. The corrective force is that of gravity under absolute control through the frame, and is the resultant of traction and extension. Traction may be augmented by weight and pulley or manually by assistants. Figures 10 to 13 show the structure of the frame.[7] It may be seen that by slowly lowering the ends of the frame the spine is gradually extended. Note the extreme upward convexity necessary to provide complete hyperextension. Formerly the yoke, intermediate between the ends of the flexible frame and over which the frame is bent, was placed opposite the kyphos. This did not always yield an extension free from discomfort to the patient. It is now placed in the region of the dorsolumbar junction so that physiologic extension of the spine may be obtained without pain.

When the apparatus is being set up, the yoke can be adjusted to the flexible frame on which the patient lies during extension, at the point where the dorsolumbar junction will rest.

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7. Dimensions: height, 5 feet and 2 inches (157.5 cm.); length, 5 feet and 10 inches (177.8 cm.); width, 3 feet (91.5 cm.); height of yoke, 3 feet and 1 inch (94 cm.); seamless steel tubing, ½ inch, 1.27 cm. (top bar, 1 inch [2.5 cm.]); length of flexible frame, 7 feet (213.3 cm.); width of flexible frame, from 18 inches to 24 inches (45.7 to 60.9 cm.); spring steel bands, 3/16 inch by 1¼ inches (0.48 by 3.18 cm.).

The width of the flexible frame can be varied so that for any patient the side bands will be at a distance of about 3 inches (7.6 cm.) from the torso. This makes it possible for the roentgenologist to place the tube and casette at the desired distances to obtain checkup roentgenograms. Furthermore, with 3 inch

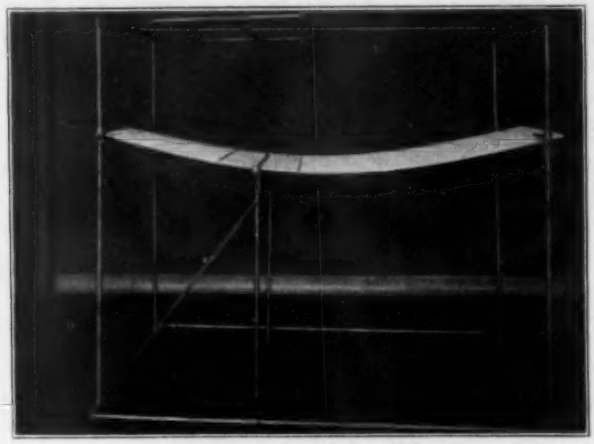

Fig. 10.—The flexible Bradford frame.

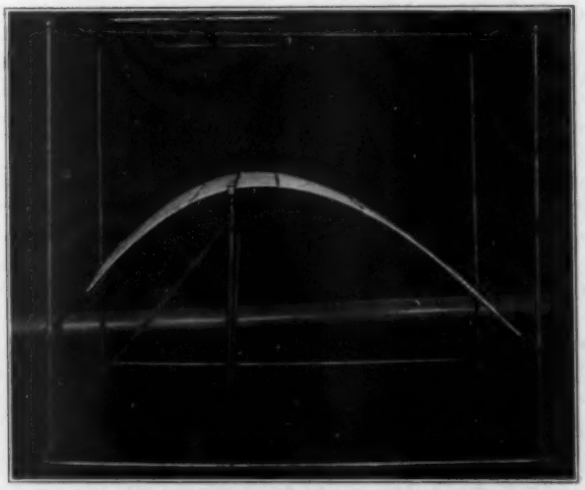

Fig. 11.—The flexible frame arranged as for spinal hyperextension.

spaces on each side of the torso, the side bands do not interfere with the application of a plaster jacket.

When it is planned to use a plaster jacket following the reduction (fig. 14), a piece of webbing about 4 inches (10 cm.) square is placed on the mattressed frame where the lumbar region will rest when the patient is placed on it. To the two sides of this piece have been sewed six 1 inch (2.5 cm.) webbing

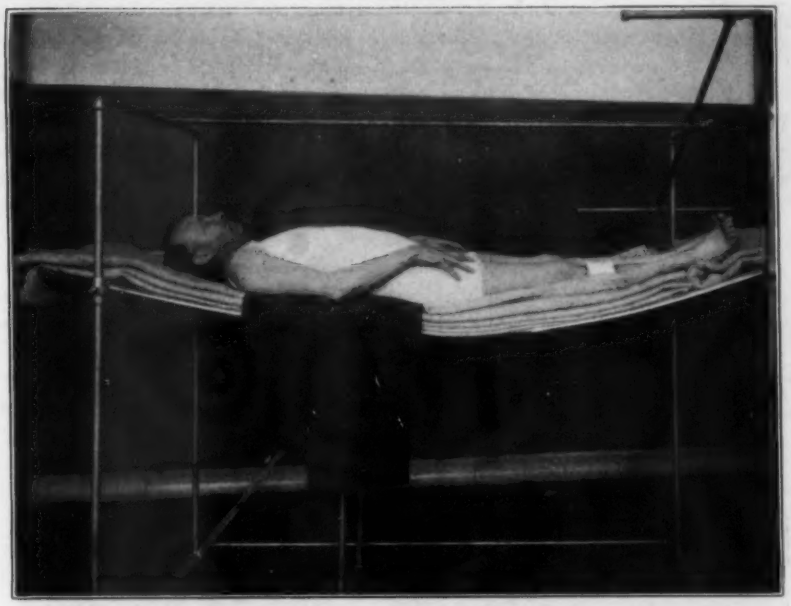

Fig. 12.—The patient properly placed on the flexible frame, yoke at the dorso-lumbar junction, and a mattress of blankets arranged, with webbing in place.

Fig. 13.—Note the extreme upward convexity necessary to provide complete hyperextension.

straps about 1 foot (33 cm.) long, three on a side, and each equipped with a buckle. The four straps at the corners of the square are sewed obliquely; the two at the middle, at right angles to the sides. Over this is placed the felt padding for the jacket, and the patient is then laid on the frame. As quickly as hyperextension has been obtained, these six straps are fixed through buckles to corresponding straps fastened to the adjustable overhead piece and tightened. The segment of the canvas covering of the frame underlying the vertebral column from the middorsal to the midsacral region is now removed from beneath. The patient's torso is thus made easily accessible for the application of the jacket while it is still maintained in hyperextension.

The technic of reduction has been radically changed since it was first described [4b] in 1930. Extension was then carried out slowly, so that the first correction in July 1928 was found by roentgenogram after fourteen days of gradual

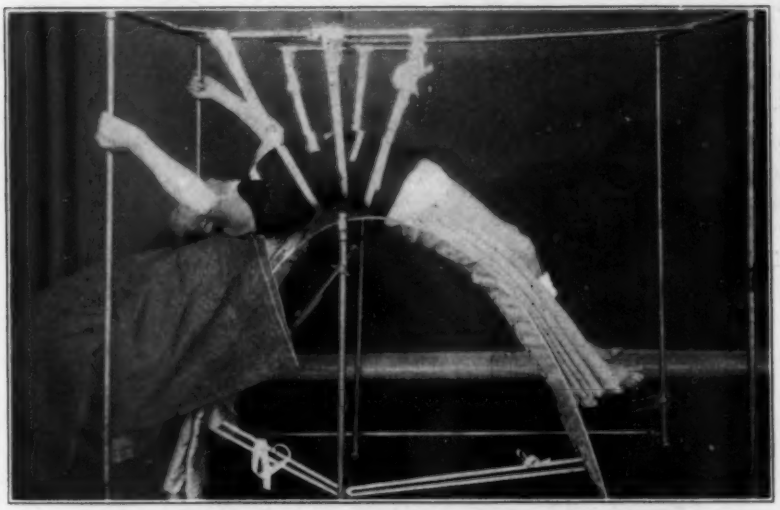

Fig. 14.—The application of a plaster jacket requires that the patient be suspended while still in extension.

extension. The rate of extension after this case was accelerated to reduce the time of correction to from four to seven days. The reason for such slow extension was that injury to the cord might surely be avoided, as such impending injury would be manifest before the damage was done. With better appreciation of the mechanics of correction and of the type of case which seems to have a low factor of cord safety the time of correction has been cut down during the past eighteen months to a few minutes (from fifteen to sixty) with as satisfactory restoration as before, apparently fully as much safety and less inconvenience to the patient. There is one exception to this practice which should be definitely understood, namely, its employment in cases which fall in the fracture-dislocation group. In this group, which might be termed, from the standpoint of injury to the cord, the "potentially dangerous group," further study will be necessary before any procedure may be advocated.

General anesthesia was not necessary in the cases in this series, nor was the employment of any local anesthesia indicated. An average dose of morphine-

scopolamine, appropriate to the patient's age and weight, may be given to allay apprehension, and also to promote relaxation of the muscles, but not to render the patient insensible to questioning or to pain more definite than discomfort. This medication has proved helpful and is recommended. The canvas-covered flexible frame on which the patient lies supine is heavily mattressed with blankets. Extension is started with the frame concave upward, and only after the adjustment of the frame is such that the patient is comfortable. The lower extremities are exposed in order that reflexes may be checked from time to time, voluntary muscle action carefully watched for early paralysis, and any other manifestation of injury to the cord noted. Reflexes tested too frequently tend to fatigue, and during the latter range of extension there has been uniformly a diminution in the intensity of response in the knee jerks.

It is practically essential to the patient's comfort and cooperation that the head be kept horizontal and not dependent. To this end, head pillows are provided as extension is increased. This provides comfort without hindering extension, since the highly flexible cervical spine does not appreciably influence the dorsal and lumbar segments.

Extension is slowly and intermittently increased in small increments until the surgeon estimates that the limit of hyperextension has been reached. This limit varies widely with age, habitual posture, type and proliferative changes, all of which should be considered. A general estimate may be reached by determining the angle between two imaginary planes on the anterior aspect of the fully extended torso: the first, the mean plane of the sternum; the second, a plane passing tangent to the anterior superior spines and the two anterior-most points of the lower thoracic margins. This angle varies roughly between 45 and 60 degrees, the former in the stocky, heavy-boned type, the latter in the long, slender-boned, hypermobile type. Usually at the stage where this angle falls within these limits the patient experiences a strong limiting pull of the rectus abdominis and anterior hip muscles, and after a little more extension lumbosacral pain begins, rapidly increasing in intensity with further efforts at extension. The latter subjective manifestations are not in themselves reliable, since it is a common experience to encounter them some time before complete extension is reached, only to have them no longer felt at that degree of extension after a few minutes at a less advanced degree. When they invariably appear at the same degree of extension, obviously near the limit, at a second or third trial at further extension, the limit has probably been reached. This process of gradually obtaining the full range through intermittent applications of extending force usually takes from twenty to thirty minutes. Lateral roentgenograms may then be made with a portable unit and the wet films interpreted. The appropriate fixation is then applied while the patient is still on the frame. When this has hardened, the patient is returned to bed. The whole procedure consumes about one and one half hours.

EXPLANATORY NOTE

The reductions obtained in this series, the experiences with fixation, the roentgenographic changes noted and the end-results to date are recorded in the tables. It is hoped that in this way a fair cross-section of the experience on which the study is based will be presented. Reproductions of all the films would require so much space, and important detail in the originals would be so often lost, that the tabulation method

seems to be the only practical way of disclosing the results and correlating the findings. The reproductions shown have been selected to emphasize high points, which it is meant thereby to stress. Each print discloses one or more points discussed, and by comparing what is to be seen in it with the corresponding note in the tables the reader will be able to gage the actual experience with the series.

RESULTS IN THIRTY-ONE REDUCTIONS (TABLE I)

Roentgenograms taken following reduction in the twenty-four cases in groups 1 and 2 show almost complete correction in the matter of the shape of the body with three exceptions (cases 9, 18 and 21). In all, there remained a slight but definite deformity, in some almost imperceptible, in others more quickly recognizable. In all except one the impression could be gained that the vertebral body was diminished in size. In case 9 (July 1928) it was decided to attempt no correction of the bone but simply to carry out exercise and supportive measures, i. e., as a control. In case 18 (January 1931) extension was stopped short of completion because of the recurrence of an old strain in the lower part of the back which proved painful and apparently was caused by the extreme position. In this case, correction fell short of the foregoing standard. In case 21 (Februay 1932), through an error in hospital routine, roentgenograms were not taken the day following reduction, and on the fourth day while straining at stool the patient suffered a pulmonary embolus which almost proved fatal, and which required the removal of the jacket after the acute phase had passed.

In all cases of groups 1 and 2, with the same exceptions, no definite narrowing of the intervertebral space could be detected directly after reduction.

The fractures in group 3, the central compression type, could not be decompressed. The disk fibers, it seemed, were so disorganized as to make little if any effective traction possible. Only two such cases appeared in the series, and this experience may therefore prove not to be the rule. In case 26, the intervertebral space was restored twelve weeks after its obliteration, a common experience in the old, uncorrected cases.

The fractures in group 4, five in number, did not give consistently good results. Only two were reduced fully (cases 27 and 31). The patient in case 30 came for reduction twenty-three days after injury—apparently too late for the fracture to yield, although some correction was obtained. The patient in case 28 showed during correction temporary interruption of cord function before complete hyperextension could be obtained. The failure of correction in case 28 (March 1929), in which a four day correction was attempted, cannot be definitely explained. The patient was not cooperative.

Lapse of Time Before Patients Came for Reduction.—Reductions started within seventeen days after the date of injury were uniformly successful, and those started after seventeen days were either partially or entirely unsuccessful. The optimum time for reduction, however, is clearly during the first week.

Age of Patients (Table 3).—The youngest patient was 15 years of age. Four were in the third decade, ten in the fourth and six in the fifth. One was 63 years of age and the oldest was 64.

Apparatus Employed in Reductions.—In all cases except two the flexible frame was used to effect reductions. In case 2, the patient was simply hyperextended by placing him on the Goldthwaite irons. In case 27, the fracture was reduced by using two Bradford frames, shifting the patient back and forth from one to the other for more than fourteen days, the frames being bent farther each time.

Time of Reduction.—During the period of gradual correction, from June 1928 to June 1931, the average time of correction was seven days. Since then, the average time of correction has been about twenty minutes. Twenty of the patients were extended gradually, and ten in less than one-half hour.

Gross Appearance of Fractures.—In table 1, under the heading "Gross Appearance of Fracture, or Fracture and Dislocation," the degree of anterior wedging is estimated in terms of the approximate loss in height of the anterior surface of the vertebral body through compression. None of the patients showed beyond question compression of the posterior wall of the centrum. In only two was there lacking some evidence of fracture of one or both of the articular surfaces of the centra (cases 1 and 4), and in only two others was this indeterminate.

The term "saucerization," coined to describe the articular surface in fractures which by roentgenogram are essentially central compressions, is not applied outside group 3 in the table. Many of the other fractures showed some central compression, however, but not sufficient to make this element predominant over wedging.

Twelve patients showed no definite narrowing of the intervertebral space, either superior or inferior. In all others, the violence had unquestionably narrowed the space.

For details concerning fracture definitely demonstrable in the posterior bony processes, see table 4, under "Complications."

Cord Injury Through Reduction.—All the patients were carefully watched during correction for evidence of impending injury to the cord, especially weakness in voluntary muscle action in the lower extremities, loss of reflexes or twitching. None received local or general anesthesia. In only one case was there evidence even of interruption of cord function. Two patients (cases 28 and 30), however, gave reasons for

TABLE 1.—*Summary of Experience in Thirty-One Reductions*

Group and Case	Date	Lapse of Time Before Patient Came for Reduction, Days	Apparatus Used	Time of Reduction	Vertebrae Involved	Gross Appearance of Fracture, or of Fracture and Dislocation (Group 4)			Correction	
						Estimated Wedging of Body	Apparent Fracture of Articular Surface	Intervertebral Space	Shape of Body	Intervertebral Space
Group 1:										
1	9/17/29	13	Flexible frame	10 days	L-1	Loss of about ⅛ (anterior)	None	No definite narrowing	Almost complete	No definite narrowing
2	4/ 8/30	10	Goldthwaite irons	Few min.	L-2	Loss of about ⅓ (anterior)	Superior	No definite narrowing	Almost complete	No definite narrowing
3	12/18/30	1	Flexible frame	3 days	D-8	Loss very slight (anterior)	Superior	No definite narrowing	Almose complete	No definite narrowing
4	3/30/31	17	Flexible frame	6 days	L-1, 2, 3 and 4	Anterosuperior lip of each	L-1 None L-2 Superior L-3 Superior L-4 Superior	No definite narrowing	Almost complete	No definite narrowing
5	7/23/31	0	Flexible frame	About 20 min.	L-1	Loss of about ⅛ (lateral and anterior)	Superior	No definite narrowing	Almost complete	No definite narrowing
6	10/ 4/31	3	Flexible frame	About 20 min.	D-12	Loss of about ⅛ (anterior)	Questionable	No definite narrowing	Almost complete	No definite narrowing
7	11/12/31	14	Flexible frame	About 20 min.	D-12	Loss of about ⅛ (anterior)	Superior	No definite narrowing	Almost complete	No definite narrowing
8	11/21/31	11	Flexible frame	About 20 min.	L-2	Loss of about ¼ (anterior)	Superior	No definite narrowing	Almost complete	No definite narrowing
Group 2:										
9	7/28/28	No correction	.....	.....	L-3 and 4	L-3, none L-4, loss of about ¼ (anterior)	Both superior	Narrowed	None	None
10	9/29/28	2	Flexible frame	4 days	L-1	Loss of about ½ (anterior)	Superior	No definite narrowing	Almost complete	No definite narrowing
11	1/23/29	3	Flexible frame	8 days	D-12	Loss of about ⅛ (anterior and lateral)	Indeterminate	Narrowing	Almost complete	No definite narrowing
12	3/ 4/29	10	Flexible frame	9 days	D-12	Loss of about ⅝ (anterior)	Superior	Narrowing	Almost complete	No definite narrowing
13	3/ 9/29	9	Flexible frame	11 days	D-11	Loss of about ¼ (anterior)	Both	Narrowing	Almost complete	No definite narrowing
14	11/30/29	1	Flexible frame	9 days	L-1	Loss of about ⅛ (anterior)	Superior	Narrowing	Almost complete	No definite narrowing
15	2/18/30	8	Flexible frame	20 days	D-12	Loss of about ¼ (anterior)	Superior	Narrowing	Almost complete	No definite narrowing
16	9/18/30	11	Flexible frame	4 days	D-11	Loss of about ¼ (anterior)	Inferior	Narrowing	Almost complete	No definite narrowing

17	10/ 8/30	5	Flexible frame	7 days	L-1	Loss of about ½ (anterior)	Superior	No definite narrowing	Almost complete	No definite narrowing
18	1/ 2/31	4	Flexible frame	3 days	L-1, D-6, 7 and 8	Loss of about ½ (anterior) (dorsal vertebrae negligible)	Superior	Narrowing	Not complete; still slight wedging	Slight narrowing
19	2/11/31	5	Flexible frame	17 days	L-3	Loss of about ½ (anterior)	Both	Narrowing	Almost complete	No definite narrowing
20	6/ 2/31	8	Flexible frame	About 20 min.	L-2	Loss of about ½ (anterior)	Both	No definite narrowing	Almost complete	No definite narrowing
21	2/11/32	12	Flexible frame	About 20 min.	L-1 and 2	Loss of about ½ (anterior)	L-1 Superior L-2 Both	Narrowing	No films; next day, pulmonary embolus; recovery	
22	4/29/32	11	Flexible frame	About 20 min.	D-12	Loss of about ½ (anterior)	Superior	Narrowing	Almost complete	Almost normal
23	5/16/32	3	Flexible frame	About 20 min.	L-1	Loss of about ½ (anterior)	Both	Narrowing	Almost complete	No definite narrowing
24	7/ 6/32	2	Flexible frame	About 20 min.	L-2	Loss of about ½ (anterior)	Superior	Narrowing	Almost complete	No definite narrowing
Group 3:										
25	9/ 9/30	9	Flexible frame	10 days	L-1	None; saucerization	Both	Narrowing	No change	No change
26	12/27/30	12 wks.	Flexible frame	26 days	L-2	None; saucerization	Superior	Obliteration	No change	No definite narrowing

						Gross Fracture—Dislocation				Correction		
						Wedging of Body	Apparent Fracture of Articular Surface	Intervertebral Space	Dislocation	Shape of Body	Intervertebral Space	Dislocation
Group 4:												
27	6/21/28	0	Bradford frames	14 days	L-1 and 2	Anterosuperior lip, L-2	Anterosuperior lip only	Obliterated	Anterior L-1 on L-2, about ⅓	Almost complete	Very slight narrowing	Complete reduction
28	3/ 5/29	1	Flexible frame	4 days	D-11 and 12	Loss of about ⅓, D-12 (anterior)	Superior	Obliterated	Anterior D-11 on D-12, about ⅓	Partial	No definite narrowing	Not reduced
29	6/30/29	2	Flexible frame	13 days	D-12, L-1	Loss of about ½, L-1 (anterior)	Superior	Obliterated	Anterior and to right D-12 on L-1, about ⅓	No change	Slight	Not reduced
30	9/20/29	23	Flexible frame	15 days	D-11 and 12	Loss of about ½, D-11 (anterior)	Superior	Obliterated	Anterior D-11 on D-12, about ¼	Slight	Slight	Not reduced
31	10/23/39	12	Flexible frame	4 days	L-1 and 2	Anterosuperior lip; loss of about ⅓ (lateral)	Superior	No definite narrowing	Anterior and lateral L-1 on L-2, about ⅓	Almost complete	No definite narrowing	Complete reduction

being on guard, and served to emphasize the advantage of having the patient conscious during reduction.

It has not been determined definitely how impending or beginning injury to the cord through extension manifests itself. The answer to this question may, however, lie in the experience with these two patients, which seems to indicate that local pain at the site of fracture precedes injury to the cord through reduction, and that loss of reflexes is the next manifestation.

The patient in case 28 (fig. 15) had severe compression fracture of the twelfth dorsal vertebra, associated with forward dislocation of the eleventh dorsal vertebra. Extension was started on the day following the accident. During a very slow extension over a period of four days definite local pain developed at the site of

Fig. 15.—Roentgenograms in case 28: *A*, appearance before reduction; *B*, appearance following reduction; *C*, end-result after four years.

the fracture and dislocation, with decided paralysis of the lower extremities and acute gastro-intestinal symptoms characterized by abdominal distress, vomiting and distention. There was no sphincter disturbance or sensory change. These observations were checked by members of the neurologic staff. Further extension was stopped, and the degree of extension was moderately lessened. After three days, this picture had entirely disappeared, and extension was cautiously resumed. Local pain again developed, and while it was possible slowly to increase the upward convexity of the frame to a slight degree, the pain prevented the accomplishment of any definite increase in extension. Further attempts to complete extension were abandoned. Since this episode, the patient has not had any sign of recurrence of these manifestations.

The patient in case 30 had severe compression of the twelfth dorsal vertebra, with definite forward dislocation of the eleventh dorsal vertebra on the twelfth. The injury occurred twenty-two days before the patient was brought to the service. Extension was started twenty-three days after the injury. It proved

uncomfortable from the start. It was continued until partial reduction was obtained. At this point, the local pain became intolerable and extension was stopped. While the patient revealed no loss of knee jerks and no paralysis, further extension was not forced by the aid of anesthesia, and this was fortunate, for fusion of the spinal cord, which was resorted to at this point, disclosed that the inferior articular processes of the eleventh dorsal vertebra were completely dislocated from their articulating fellows of the twelfth dorsal vertebra, and lay anterior to the latter, that on the right side lying immediately anterior to and locked with the corresponding process of the twelfth dorsal vertebra. Any further extension in this case, it seems, would inevitably have resulted in compression of the cord. Following fusion, this patient made an uneventful recovery and at fourteen months returned to his preinjury activities (chain store manager) without complaint.

In no other patient was there any manifestation of either fleeting or permanent injury to the cord following reduction.

It should be noted, however, that in case 27 (fig. 9), with marked forward dislocation of the first lumbar vertebra on the second, the deformity was reduced without any manifestation of injury to the cord, either during or after reduction.

It seems probable that with careful adherence to the technic described injury to the cord will not occur during reduction in compression fractures uncomplicated by dislocation, in view of the foregoing experience, the mechanics of extension, and the added factor of safety to the cord afforded by the considerable space between it and the walls of the spinal canal in uncomplicated fracture. The definite possibility, however, of injury to the cord during reduction should never be absent from the surgeon's mind, and when dislocation is present, complicating the fracture, it is a real possibility, with local pain possibly the first warning.

APPARATUS AND TECHNIC OF FIXATION

The appliance selected for fixation must maintain hyperextension. Otherwise the deformity of the bone will recur (case 6, fig. 16). As the intervertebral disk is usually definitely narrowed or obliterated within one year after the injury, it is of utmost importance to preserve the correction until bone reorganization is adequate. Plaster of paris shells will accomplish this, but they present the decided disadvantage of keeping the patient recumbent, allowing but two positions, prone and supine. The plaster of paris jacket, correctly applied in selected cases, was the most satisfactory form of fixation employed in this series. In favorable cases the patients may be ambulatory from the start, leave the hospital at an early date and may even resume their preinjury activities, if not actually laborious. In this way, general muscle tone is preserved throughout the period of treatment, and morale is decidedly better (fig. 17, case 17).

The patients suitable for ambulatory treatment in a jacket directly after correction are those in whom the fractured vertebra or vertebrae are situated in a portion of the spinal column which is convex forward, as the second, third or fourth lumbar segments. Occasionally, the anterior convexity extends as high as the tenth or eleventh dorsal segment. Such vertebrae, in the erect attitude

and extreme hyperextension of the column, receive the superincumbent weight on the posterior portion of the body (fig. 18). A careful checking of the vertebrae by frequent roentgenograms taken through windows in the jacket has failed to disclose any appreciable loss of bone correction under conditions of constant stress while the wearer was up and about, walking and riding in an automobile. Some ambulatory patients, when overtired, experienced lumbosacral backache (five of twenty-eight, or 18 per cent). Curtailment of activities controlled this complication. One of those so treated began to have, after being up and about for several

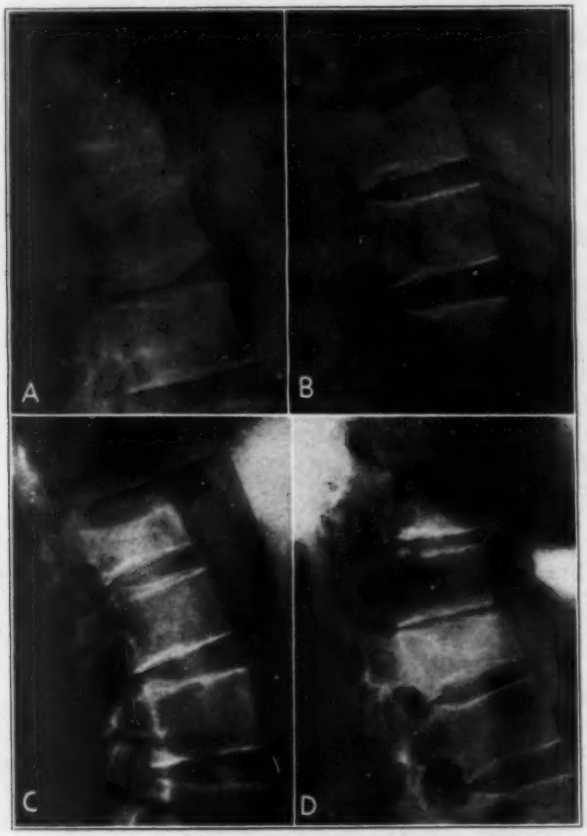

Fig. 16.—Roentgenograms in case 6, in which the correction was lost in a plaster jacket that had become loose owing to the patient's loss of weight: *A*, before reduction; *B*, after reduction; *C*, loss of correction in the jacket; *D*, end-result after sixteen months.

weeks, pain over the posterior sacro-iliac ligaments on one side, with referred pain in the posterior thigh and calf on the same side, requiring that he adopt a less strenuous manner of living. This tendency disappeared on completion of the period of protection of the vertebra and resumption of normal posture.

The patients definitely unsuited to this treatment are those whose fractures lie in the anteriorly concave middle and upper dorsal region (case 16, table 2). This

concavity in some spines extends as far down as the second lumbar vertebra; hence no definite dividing line can be set, but each case must be determined according to the stresses to which the fractured vertebra will be subjected in the hyperextended position. Patients whose fractures have resulted in crushing of the posterior portion of the centrum or in lateral wedging are obviously not suited to ambulatory treatment. Furthermore, failure is apt to follow such practice in obese persons, and indeed all patients receiving ambulatory treatment should be carefully watched for loss of weight sufficient to allow flexion (case 6, fig. 16). A jacket which for any cause is loose should be removed and either a new one applied or the ambulatory treatment abandoned. Probably a jacket on a recumbent patient maintains correction in all vertebrae up to and possibly including the eighth dorsal. My experience in this manner of fixation is too limited to state—two patients—in both of whom correction was preserved until reorganization of the

Fig. 17.—Roentgenograms in case 17: *A*, spinal column while patient was under ambulatory treatment in a jacket applied directly after reduction and worn six months; *B*, the end-result after two years and four months.

bone was complete (fig. 19, case 20). It seems to be a question when recumbency is demanded which is more acceptable to the patient, a jacket or shells.

The support of corrected vertebrae in cases unsuited to jackets, and in cases of spinal fusion, is conveniently afforded by plaster shells. Patients in such cases should be placed immediately on a regimen of exercises: active extension for the maintenance and development of the erectores spinae, abdominal retraction and deep breathing, and for the lower extremities mild "goose-stepping."

Technic of the Application of a Jacket.—The patient, with spine fully hyperextended and torso equipped with shirt or stockinet and protected by felt, is partially suspended while still on the frame by the small webbed square, already described, under the lumbar region (fig. 14). Heavy felt padding is essential. Two thicknesses of half inch (1.27 cm.) saddlers' felt are used over the spinal

column and one layer of fourth inch (0.64 cm.) or thicker felt over the iliac crests and about the upper part of the thorax, as shown in figure 21 *B* and *C*. Goldthwaite irons, adjusted to fit the contour of the hyperextended spine, are then placed beneath the patient's torso, the suspending canvas sling is removed, and the plaster applied (fig. 20). This simplification is a convenience. Equally practical it is to transfer the patient at the completion of extension to the standard form of Goldthwaite irons as shown in figure 21. The jacket should be about one-fourth inch thick. It is extended as high as the suprasternal notch, is applied snugly over the entire anterior wall of the chest and is molded snugly to the iliac

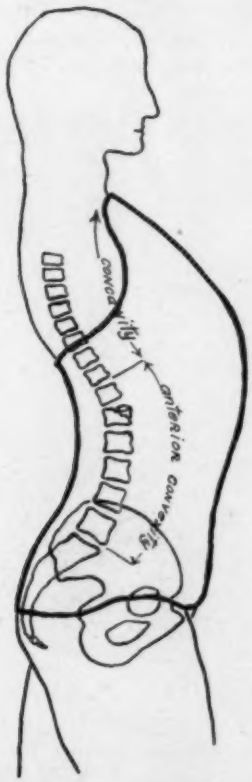

Fig. 18.—Drawing showing the type of patient suited to ambulatory treatment in a jacket. The fractured vertebra (or vertebrae) is situated in a portion of the spinal column which is convex forward. Such a vertebra in the erect attitude and extreme hyperextension of the column receives the superincumbent weight on the posterior portion of the body.

crests, reaching as far down as about one-half inch below the anterior superior iliac spines. Posteriorly, it fits snugly into the lumbar lordosis and extends from the spines of the scapulae to half way down the sacrum. Three areas of accurate contact should thus result, two anteriorly, namely, the anterior wall of the chest and the anterior portion of the iliac crests, and one posteriorly, the lumbar region. When dry, the jacket is trimmed, and the patient is returned to bed.

Fig. 19.—Roentgenograms illustrating maintenance of correction during recumbency in a jacket: *A*, before reduction; *B*, after four months of recumbency in a jacket.

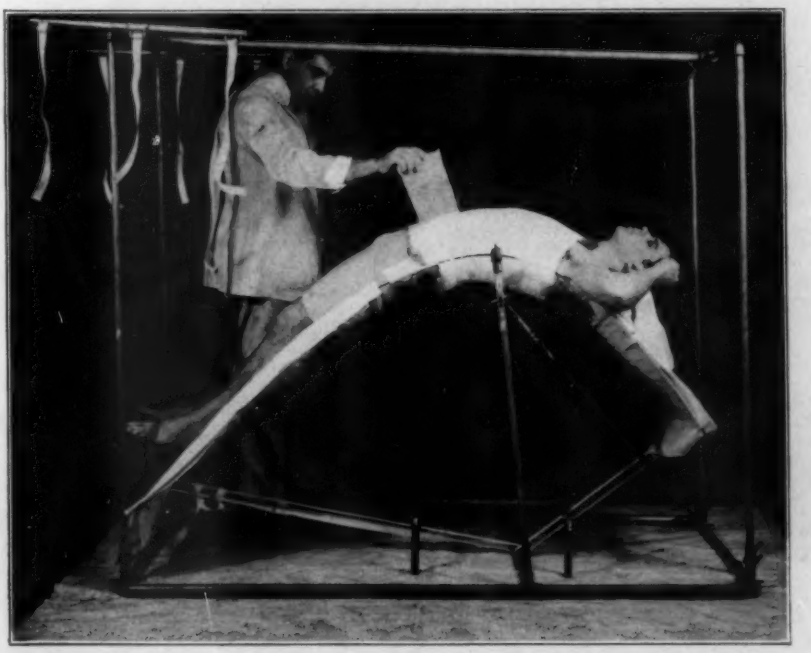

Fig. 20.—Here a plaster jacket has been applied following reduction.

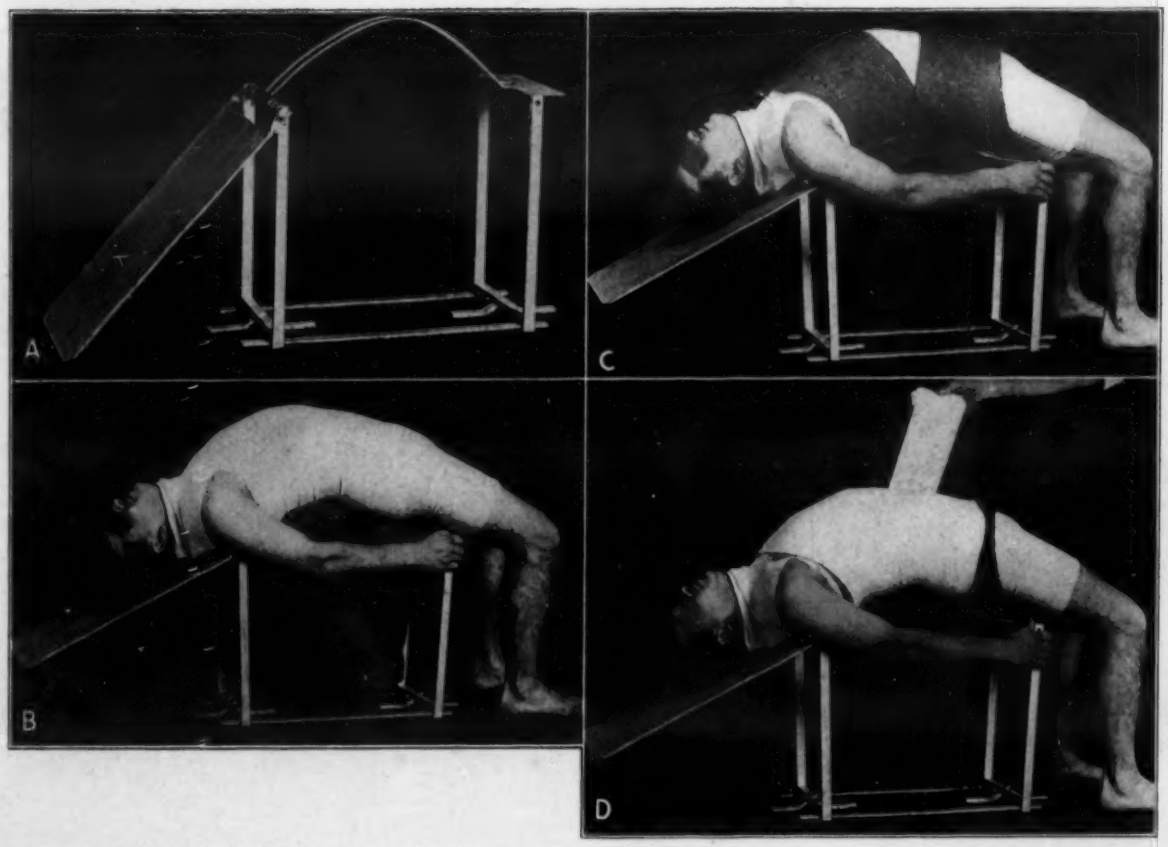

Fig. 21.—*A*, the Goldthwaite irons used in application of the plaster jacket; *B* and *C*, arrangement of saddiers' felt; *D*, application of the jacket.

It is well to place the patient on a diet of fluids and give a daily enema for forty-eight hours following correction and application of the jacket. Otherwise, gastro-intestinal upsets are common; in two patients in this series adynamic ileus developed. In the very slender and the old, it may be necessary to split the jacket in the midline anteriorly and spread it a little to allay a distressing feeling of smothering, evidently associated with the extreme expansion of the chest. Both patients with ileus promptly lost their symptoms following this procedure. Later the jacket may be brought together and wrapped, or wrapped less tightly, with several layers of plaster bandage. Windows cut the following day in the sides of

Fig. 22.—The completed jacket, ready to have windows cut in it opposite the fracture.

the jacket, opposite the fracture, make possible roentgenographic interpretation of progress (fig. 22). It has been the custom to have roentgenograms taken the day following the application of the jacket, one week afterward, and if these were satisfactory, once a month thereafter until reorganization of the bone seemed assured.

Following the period of fixation in plaster, which lasts until reorganization of the bone is assured (from two to seven months), a high spring steel back-brace is applied while the patient is in the hyperextended position. This is worn

diers' felt; *D*, application of the jacket.

while the patient is up and about, and is removed when he is recumbent. Extension exercises are vigorously pushed at this stage, so that in from one to two months the erectores spinae are powerful and fully capable of performing their task. The brace is worn until the strength of the muscles is definitely adequate, usually from the fifth to the seventh month, and is then gradually discarded over a period of from two to three weeks. A deep lumbar lordosis remains which must be corrected before the active stage of treatment can be regarded as over. If it is not corrected, the patient is theoretically fully as liable to strain and fatigue as if the fractured vertebra had not been corrected. This may be accomplished in from two to four weeks, or more, varying with the patient's age and ability to cooperate. Exercises in lumbar flexion are given to stretch contracted lumbar soft parts, and the patient is instructed in pelvic control and the habitual carriage of the pelvis in the vertical position. The restoration of back mechanics and the repair of the fracture being completed, it is simply a question of general development when the successful return to preinjury activities may be expected.

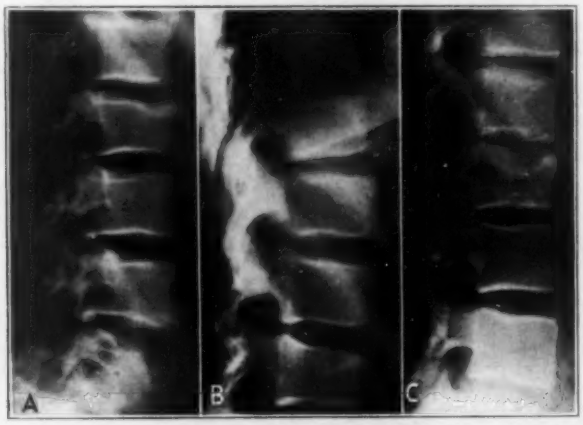

Fig. 23.—Roentgenograms in a case of nuclear prolapse (case 24): *A*, before reduction; *B*, after reduction; *C*, nuclear prolapse at seven months.

RESULTS IN THIRTY-ONE FIXATIONS (TABLE 2)

Jacket-Recumbency.—Eight patients whose fractures were fixed by recumbency in a jacket for from one to seven days suffered no loss of correction of either vertebral body or intervertebral space. Four others so treated for three weeks, six weeks, two and four months, respectively, likewise retained full correction.

Jacket-Ambulatory.—Fourteen patients were rendered ambulatory in jackets from one to seven days following the correction, and this type of fixation was continued for from two to seven months, varying with the severity of their deformity and apparent disorganization of the bone (an average of four and one-half months). Of this group two lost the bone correction (cases 6 and 16). In the others, bone correction

was maintained. The patient in case 6 (fig. 16), after almost complete correction, was discharged from the hospital seven days following reduction, having been ambulatory for three days, with orders to return for checkup at two week intervals. She did not report until thirteen weeks later, when she had lost about 20 pounds (9.1 Kg.) and her jacket was quite loose through that circumstance. Roentgenograms disclosed the loss of correction. In retrospect, she should not have been selected for ambulatory treatment because of her initial obesity and the site of her fracture, the twelfth dorsal vertebra, which in her case lay at the beginning of the anteriorly concave dorsal curve, and because of the doubt of her willingness to come in for frequent observation. The patient in case 16, likewise ill-selected for ambulatory-jacket care, could not, through circumstances, be closely watched, and she lost her correction following a second and unsatisfactory application of a jacket.

The fate of the intervertebral space was, however, quite different. There was definite narrowing during this period in three patients, marked narrowing in three, and the space was lost, of course, in the two patients in whom bone correction was not maintained. In only six patients were both bone and space correction maintained. Of these, it should be stated that three lost their spaces subsequent to bone repair and termination of fixation, and one showed a slight narrowing of the space at two years and four months, which was evidently to remain indefinitely by reason of a complete and heavy bridge of bone.

Shells.—Shells were used in eleven cases, and the restoration of both bone and space was preserved throughout their period of fixation.

FATE OF INTERVERTEBRAL DISK AND FRACTURED VERTEBRAL BODY (TABLE 3)

The inevitable alteration in structure of the disk following extensive injury was clearly demonstrated at Schmorl's clinic. With alteration in structure there ensues change in function in the form of loss of adaptability to changing stresses and of resistance to "wear and tear." Local mechanics are no longer adequate to demands, and compensatory structural changes slowly develop similar to those observed in other injured weight-bearing joints, namely, narrowing of the joint space, proliferative bone changes at the margins of the joint and increased bone density. These changes and their development may be easily followed by means of a series of roentgenograms of the patient, taken monthly at first and then at six month intervals. Figure 6 illustrates the changes in a typical case. They vary with age, occupation and previous condition of the joints.

Spur Formation.—This occurred in eighteen cases, or 60 per cent, and was first noted at various times from five weeks to four and one-

TABLE 2.—*Summary of Experience in Thirty-One Fixations*

Group and Case	Date	Vertebra Involved	Type of Fixation		Loss of Correction		Type of Fixation		Loss of Correction		Type of Fixation		Loss of Correction	
			First	Time	Vertebral Body	Intervertebral Space	Second	Time	Vertebral Body	Intervertebral Space	Third	Time	Vertebral Body	Intervertebral Space
Group 1:														
1	9/17/29	L-1	Jacket, recumbent	6 days	None	None	Jacket, ambulatory	8 wks.	None	None	High back-brace	3 mos.	None	None
2	4/ 8/30	L-2	Jacket, recumbent	2 mos.*	None	None	Jacket, ambulatory	2 mos.	None	None	High back-brace	6 mos.	None	None
3	12/18/30	D-8	Jacket, recumbent	1 day	None	None	Jacket, ambulatory	2 wks.	None	Definite narrowing	Jacket, ambulatory	5 mos.	None	No further narrowing
4	3/30/31	L-1, 2, 3 and 4	Jacket, recumbent	1 day	None	None	Jacket, ambulatory	4 mos.	None	None	High brace	7 wks.	None	None
5	7/23/31	L-1	Jacket, recumbent	6 wks.†	None	None	Jacket, ambulatory	2 mos.	None	None	High brace	3 mos.	None	Very slight narrowing
6	10/ 4/31	D-12	Jacket, recumbent	5 days	None	None	Jacket, ambulatory	4 mos.	Correction lost‡	Marked narrowing	High brace	2 mos., then intermittent	Complete	Marked narrowing
7	11/12/31	D-12, L-1	Jacket, recumbent	5 days	None	None	Jacket, ambulatory	4 mos.	None	Marked narrowing	High brace	6 wks.	None	Definite narrowing
8	11/12/31	L-2	Jacket, recumbent	4 days	None	None	Jacket, ambulatory	5 mos.	None	Marked narrowing	High brace	3 wks.	None	None
Group 2:														
9	7/28/28	L-3, L-4	Jacket, recumbent		No correction									
10	9/29/28	L-1	Shells (fusion operation; jacket, recumbent)	5 wks.‖	None	None	Jacket, ambulatory	10 wks.	None	Very slight narrowing	High brace	7 wks.	None	Very slight narrowing
11	1/23/29	D-12	Shells	8 wks.	None	None	Jacket, ambulatory	8 wks.	None	None	High brace	4 wks.	None	Definite narrowing at 6 mos.
12	3/ 4/29	D-12	Shells	8 wks.	None	None	Jacket, ambulatory	2 mos.	None	Very slight narrowing	High brace	5 mos.	None	Marked narrowing
13	3/ 9/29	D-11	Shells	5 wks.	None	None	Jacket, ambulatory	6 wks.	None	Very slight narrowing	High brace	6 wks.	None	Very slight narrowing
14	11/30/29	L-1	Jacket, recum-	3 days	None	None	Jacket, ambu-	4 mos.	None	Definite	High brace	8 wks.	None	Marked nar-

14	11/30/29	L-1	Jacket, recumbent	3 days	None	None	Jacket, ambulatory	4 mos.	None	Definite narrowing	High brace	8 wks.	None	Marked narrowing
15	2/18/30	D-12	Jacket, ambulatory	3 mos.	None	Marked narrowing	.....	.....	.....	.....	High brace	3 mos.	None	
16	9/18/30	D-11	Jacket, ambulatory	7 wks.	None	None	Second jacket	6 wks.	Correction	Correction lost‡	High brace	3 mos.		
17	10/ 8/30	L-1	Jacket, ambulatory	6 mos.	None	Slight	.....	.....	.....	.....	High brace	3 mos.	None	None
18	1/ 2/31	L-1	Jacket, ambulatory	3 mos.	None	None	.....	.....	.....	.....	High brace	3 mos.	None	Complete
19	2/11/31	L-3	Shells	3 mos.‖	None	None	Jacket, ambulatory	3 mos.	None	None	High brace	6 wks.	None	None
20	6/ 2/31	L-2	Jacket, recumbent	4 mos.#	None	None	.....	.....	.....	.....	High brace	3 mos.	None	None
21	2/11/32	L-1 and 2	Fixation removed because of pulmonary embolus		Correction lost									
22	4/29/32	D-12	Shells	5½ mos.	None	None	.....	.....	.....	.....	High brace	2 mos.	None	None
23	5/16/32	L-1	Shells	2 mos.	None	None	Jacket, ambulatory	2 mos.	None	Definite in upper	High brace	2 mos.	None	Definite in both
24	7/ 6/32	L-2	Jacket, ambulatory	4 mos.	None	Definite	.....	.....	.....	.....	High brace	2 mos.	None	Marked
Group 3:														
25	9/ 3/30	L-1	Jacket, recumbent	2 days	None	No correction	Jacket, ambulatory	6 mos.	None	No correction	High brace	2 mos.	None	No correction
26	12/27/30	L-2	Jacket, ambulatory	7 mos.	.....	None	.....	.....	.....	.....	High brace	3 mos.	None	Marked
Group 4:														
27	6/21/28	L-2	Shells	3 mos.‖	None	None	.....	.....	.....	.....	High brace	6 mos.	None	Definite
28	3/ 5/29	D-12	Shells	3½ mos.	None	None	Jacket, ambulatory	4 mos.	None	Definite	Corset	5 mos.	None	Marked
29	6/30/29	L-1	Shells	5 wks.	.....	None	Jacket, ambulatory	4 wks.	.....	Marked	High brace	3 mos.		
30	9/20/29	D-12	Shells	3 mos.‖	.....	None	Jacket, ambulatory	3 mos.	.....	None	High brace	4 mos.	.....	Definite
31	10/23/30	L-2	Jacket, ambulatory	3½ mos.	None	None	.....	.....	.....	.....	High brace	3 mos.	.....	Definite

* Extensive fracture at ankle.
† Fracture of os calcis.
‡ See results in fixation (table 6).
# Extensive fracture, both ankles.
‖ Spinal fusion.

TABLE 3.—*Roentgenographic Changes*

Case	Date	Vertebra Involved	Age	Occupation	Spurring: Before	Spurring: New Spur Formation: First Noted	Spurring: New Spur Formation: Still Increasing	Spurring: New Spur Formation: Bridging Complete	Time of Apparent Union	Time of Loss of Intervertebral Space*: First Noted: During Fixation	Time of Loss of Intervertebral Space*: First Noted: After Fixation	Time of Loss of Intervertebral Space*: Fixed: Time	Time of Loss of Intervertebral Space*: Fixed: Amount	Time of Loss of Intervertebral Space*: Fixed: Complete	Apparent Nuclear Prolapse
1	9/17/29	L-1	31	Salesman	None	None (3 yrs., 5 mos.)	.....	.....	Indeterminate	None	None (3 yrs., 5 mos.)	.....	.....	.....	None
2	4/ 8/30	L-2	64	Bricklayer	Extensive D-10 and 11, moderate lumbar	None (2 yrs., 9 mos.)	.....	.....	4 mos.	None	None (2 yrs., 9 mos.)	.....	.....	.....	Slight L-4 (first noted 2 yrs., 9 mos.)
3	12/18/30	D-8	22	Telephone linesman C†	None	None (2 yrs.)	.....	.....	2-5 mos.	2 wks.	.....	2 wks. (more than 2 yrs.)	About ½	.....	None
4	3/30/31	L-1, 2, 3 and 4	23	Longshoreman, C	None	None (1 yr., 11 mos.)	.....	.....	4 mos.	None	None (1 yr., 11 mos.)	.....	.....	.....	L-2 and 3 (4 mos.)
5	7/23/31	L-1	56	Janitor	None	None (1 yr., 6 mos.)	.....	.....	4-7 mos.	None	Between 7-13 mos.	13 mos. (more than 5 mos.)	Slight	.....	Questionable (4-13 mos.)
6	10/ 4/31	D-12	50	Housekeeper	Moderate lateral	None (1 yr., 4 mos.)	.....	.....	4-7 mos.	4 mos.	.....	4 mos. (more than 12 mos.)	About ⅔	.....	None
7	11/12/31	D-12 L-1	33	Registered nurse	None	None (1 yr., 1 mo.)	.....	.....	2½ mos.	None	Between 5-7 mos.	7 mos. (more than 6 mos.)	About ½	.....	None
8	11/12/31	L-2	56	Builder	None	Slight (14 mos.)	?	.....	5 mos.	None	None (1 yr., 2 mos.)	.....	.....	.....	None
9	7/28/28	L-3 L-4	22	Carpenter	None	None	.....	.....	3 mos.	.....	.....	Onset	About ½	.....	None
10	9/20/28	L-1	36	Carpenter	None	6 mos.	16 mos.	4 yrs., 4 mos.	Indeterminate	15 wks.	.....	5 mos. (more than 3 yrs., 11 mos.)	About ½	.....	None
11	1/28/29	D-12	39	Freight-handler, C	None	8 mos.	.....	14 mos.	Indeterminate	None	Between 4-7 mos.	7 mos. (more than 3 yrs., 5 mos.)	About ¾	.....	None
12	3/ 4/29	D-12	36	Housewife	None	1-4 yrs.	.....	4 yrs.	Indeterminate	3½ mos.	.....	11 mos.	Complete loss	11 mos.	None
13	3/ 9/29	D-11	44	Sportswoman	Slight lipping L-1 and 2	4 yrs.	.....	.....	4 mos.	None (4 mos.)	4 yrs.	.....	Marked	.....	None
14	11/30/29	L-1	41	Fireman, C	None	6 mos.	3 yrs., 2 mos.	.....	3½-5 mos.	3 wks.	.....	6 mos.	.....	6 mos.	None
15	2/18/30	D-12	63	Cook	None	None (more	.....	.....	3-4 mos.	2 wks.	.....	4 mos.	.....	4 mos.	L-1

15	2/18/30	D-12	63	Cook	None	None (more than 3 yrs.)	.....	.....	3-4 mos.	2 wks.	.....	4 mos.	.....	4 mos.	L-1
16	9/18/30	D-11	58	Housewife	None	None (more than 7 mos.)	Not known	Not known	Indeterminate	1-3 mos.	.....	3 mos.	Complete	3 mos.	?
17	10/ 8/30	L-1	51	Farmer	Moderate	4-5 mos.	10 mos.	Indeterminate	Indeterminate	5 mos.	None	5 mos. (more than 2 yrs.)	Slight	.....	None
18	1/ 2/31	L-1	24	Sportswoman	None	None	.....	.....	Indeterminate	None	6 mos.	6 mos.	Complete	6 mos.	None
19	2/11/31	L-3	36	Boatbuilder, C	Marked dorsal	3 mos.	2 yrs.	Upper, 2 yrs.; lower, none	8-11 mos.	None	.....	.....	.....	.....	None
20	6/ 2/31	L-2	47	Steeplejack	Slight	10 wks.	7 mos.	18 mos.	10 wks.	None	2½-7 mos.	7 mos. (more than 20 mos.)	About ⅛ upper space, about ⅛ lower space	.....	Questionable
21	2/11/32	L-1, 2	49	R. R. freight conductor, C	None	7 mos.	10 mos.	.....	3 mos.	.....	2 mos.	D-12, 7 mos., L-1, 2 mos. (more than 10 mos.)	About ⅛ upper space	Complete	L-1, L-2
22	4/29/32	D-12	46	Housewife	Slight calcification of anterior ligament	None (more than 9 mos.)	.....	.....	4 mos.	None	7-9 mos.	?	About ½	.....	None
23	5/16/32	L-1	34	Tree surgeon's assistant, C	None	9 mos.	.....	.....	6 mos.	2 mos.	7 mos.	?	Upper ⅔ Lower ½	.....	Probable
24	7/ 6/32	L-2	15	Student	None	None (more than 7 mos.)	.....	.....	3 mos.	4 wks.	6 mos.	6 mos. (more than 2 mos.)	Upper ½ Lower ¼	.....	Inferior portion L-2
25	9/ 3/30	L-1	52	Station fireman, C	None	5 wks.	.....	8 mos.	4-8 mos.	Never restored	.....	.....	.....	.....	None
26	12/27/30	L-2	46	Porter, C	None	10 mos.	.....	13 mos.	Indeterminate	None	8 mos.	10 mos.	.....	10 mos.	None
27	6/21/28	L-1 L-2	32	Milkman, C	None	4 wks.	3-4 yrs.	3 yrs., 4½ yrs.	3-5 mos.	3 mos.	None	3 mos. (more than 4 yrs., 3 mos.)	About ½	.....	None
28	3/ 5/29	D-11 D-12	38	Scrubwoman, C	None	3 yrs. (very slight)	? 4 yrs.	.....	6-8 mos.	3-5 mos.	.....	5 mos.	.....	5 mos.	D-12
29	6/30/29	D-12 L-1	18	Mechanic	None	.....	3 yrs., 7 mos.	1 yr., 3 mos.	?	7-12 wks.	.....	.....	.....	7-12 wks.	None
30	9/20/29	D-11 D-12	39	Chain store manager	None	8 mos.	?	8 mos.	8 mos.	3-4 mos.	None (more than 3 mos.)	3-4 mos.	About ½	.....	None
31	10/23/30	L-1	46	Mechanic	Moderate	?	?	4 mos.	Indeterminate	None	Yes	2 yrs., 3 mos.	About ½	.....	None

* Refers to time after reduction.

† C means that compensation was sought.

half years. In sixteen of these eighteen cases there was narrowing of the intervertebral space; in two, narrowing was not definite. Of the latter two, one was that of a man, aged 56, doing laborious work; in the other there had been surgical fusion. Eight other patients showed marked narrowing but spurs did not develop. Of these eight, three were 15, 22 and 24 years of age, respectively; three were women of light activities; one had not had roentgenograms taken, because of other illness confining her to bed, and in the fifth the narrowing was too recent (nine months). With loss of the intervertebral disk and alteration of the size and shape of the vertebral body, local mechanics are inadequate and these proliferative reparative changes ensue.

TABLE 4.—*Time for Complete Bridging of Intervertebral Space*

Case	Time of Recognition	Case	Time of Recognition
31	4 mos.	20	18 mos.
25	8 mos.	19	2 yrs.
30	8 mos.	27	3 yrs. and
26	13 mos.		4 yrs., 6 mos.
11	14 mos.	12	4 yrs.
29	15 mos.	10	4 yrs., 4 mos.

TABLE 5.—*Narrowing of Intervertebral Space*

Narrowing of Space	Number of Cases	Percentage
Slight	3	10
About ½	10	32
About ⅔	2	6
About ¾	2	6
Complete	9	29

Complete Bridging of Intervertebral Space by Bone.—This condition apparently resulted in fusion in eleven of twenty-six cases, or 42 per cent, as shown by roentgenograms. The time of probable completion of the bridge across the intervertebral spaces varied widely (table 4).

Narrowing of Intervertebral Space.—This change occurred in twenty-six cases, or 84 per cent. In only five was it absent, in one of which a spinal fusion was performed. No fracture of the articular surface was demonstrated in one of these five, and there probably was none, since the disk did not become narrow. I am unable to explain it in the other three, other than to assume that the cartilaginous end-plates escaped fracture, although they seemed not to have done so.

Nuclear Prolapse.—This condition was apparent or questionable in ten cases, or 32 per cent (figs. 15 and 23).

Bone Reorganization.—This condition was indeterminate by roentgenogram in ten patients, definite in nineteen in from two to seven

months, varying with the degree of disorganization of the bone, and in two other patients, with badly shattered centra, in from four to eight and eight to eleven months, respectively.

END-RESULTS (TABLE 6)

Restoration to Preinjury Activities.—Twenty patients, or 65 per cent, returned successfully to preinjury activities and remained free from pain. They returned in from two to fourteen months (the average was eight and a third months). Of this number, eight would probably generally be regarded as having had severe fractures, nine, moderately severe and three, mild. Three of the nine patients with severe fractures had surgical fusion. Five of the twenty patients were in the industrial compensation class.

Restoration of Light Activities.—Six patients returned successfully to lighter activities, five at from five to eleven months and one at twenty-seven months. Four of these patients do light work because of pain in the back on doing laborious work steadily. Of the other two, one (case 3) prefers clerical work to hard labor; the other (case 21, eleven months after injury) has been instructed not to do heavy work yet. In three, the fracture healed and was reduced; in one, an excellent reduction was obtained but later was lost during fixation (case 6) and in two there was no correction.

Failure to Return to Work.—Table 7 presents the facts regarding patients who have not resumed former occupations.

Fractures of Posterior Bony Processes.—Roentgenograms showed fracture in the bony processes, exclusive of the transverse processes, in only five of the thirty-one cases. They were confined to the articular processes and laminae. Doubtless, many were not detected. Fracture of the pedicles was not diagnosed in the entire series; five of the patients showed fractures in one or more transverse processes.

SPINAL FUSION

It may be seen that the restoration of the shape of the vertebral body and of the intervertebral space obtained by hyperextension reestablishes the preinjury anteroposterior spinal curves. This restoration is only partially maintained in a high percentage of cases (84 per cent in this series) through the loss of some or all of the intervetebral disk. It is also apparent that a large proportion (65 per cent in this series) of these patients with correction return to preinjury activities, free from symptoms, in from two to fourteen months in spite of this loss. This bespeaks a high degree of adaptability of the back as a whole to whatever loss in statics narrowing of the disk produces.

TABLE 6.—*End-Results*

Case	Vertebra	Age	Occupation*	Complications	Lumbosacral Junction	Estimate of Correction	Surgical Fusion	Period of Fixation	Apparent Fusion by Bridging	Correction of Body	Estimated Loss of Intervertebral Space	Return to Light Activities†	Return to Preinjury Activities†	Symptoms; Nature of Disability	Time of End-Result
1	L-1	31	Salesman	None	No defects	Almost complete	None	9 wks.	None	Maintained	None	.....	2 mos.	None	3 yrs., 5 mos.
2	L-2	64	Bricklayer	Fracture of ankle	Marked spurring	Almost complete	None	4 mos.	None	Maintained	None	.....	.....	None; cannot get work	2 yrs., 10 mos.
3	D-8	22	Telephone linesman, C	None	No defects	Almost complete	None	5½ mos.	None	Maintained	About ½	6 mos. (clerical)	.....	None	2 yrs.
4	L-1, 2, 3	23	Longshoreman, C	Sprain condylar fracture of femur	Failure of fusion, neural arch, 1st sacral	Almost complete	None	4 mos.	None	Maintained	None	11 mos. (dock tender)	.....	Pain in muscles in lower part of back on doing heavy lifting	1 yr., 10 mos.
5	L-1	56	Janitor	Fracture of os calcis	No defects	Almost complete	None	4 mos.	None	Maintained	Slight	.....	7 mos.	None	1 yr., 6 mos.
6	D-12	50	Housekeeper	None	Narrowing L-5 intervertebral space	Almost complete	None	4 mos.	None	Lost during fixation period	About ⅔	6 mos.	.....	Still wears brace; aches in muscles of lower part of back after much hard work	1 yr., 4 mos.
7	D-12 L-1	33	Registered nurse	None	No defects	Almost complete	None	4 mos.	None	Maintained	About ½	.....	3 mos.	None	1 yr.
8	L-2	56	Builder	None	No defects	Almost complete	None	5 mos.	None	Maintained	None	6 mos.	9 mos.	None	1 yr., 2 mos.
9	L-3 L-4	22	Carpenter, C	None	No defects	None	None	None	None	No correction	About ½ (both)	None	None	Aches in muscles in lower part of back when tired	3 yrs., 6 mos.
10	L-1	36	Carpenter	None	No defects	Almost complete	D-12 L-1 and 2	4½ mos.	Yes	Maintained	About ½	8 mos.	10 mos.	None	4 yrs., 4 mos.
11	D-12	39	Freight-handler, C	None	No defects	Almost complete	None	4 mos.	Yes	Maintained	About ¾	.....	13 mos.	None	4 yrs.
12	D-12	36	Housewife	Fracture of	No defects	Almost	None	4 mos.	Yes	Maintained	Complete			None	

12	D-12	36	Housewife	Fracture of lamina and superior articular process, D-12	No defects	Almost complete	None	4 mos.	Yes	Maintained	Complete	.....	10 mos.	None	3 yrs., 11 mos.
13	D-11	44	Sports-woman	None	No defects	Almost complete	None	4½ mos.	None	Maintained	Marked	.....	4 mos.	None	3 yrs., 10 mos.
14	L-1	41	Fireman, C	Fracture of transverse process, L-1	No defects	Almost complete	None	4 mos.	None	Maintained	Complete	2 wks. (telephone operator)	7 mos.	None	3 yrs., 2 mos.
15	D-12	63	Cook	Syphilis, arterio-sclerosis	Partial sacraliza-tion, L-5 transverse process	Almost complete	None	4 mos.	None	Maintained	Complete	.....	9 mos.	None	2 yrs., 11 mos.
16	D-11	58	Housewife	Fracture of left ulna, Raynaud's disease	No defects	Almost complete	None	4 mos.	Not known	Lost during fixation period	Complete	.....	10 mos.	Ache in mus-cles in lower part of back when tired	2 yrs., 4 mos.
17	L-1	51	Farmer	Fracture of radius	No defects	Almost complete	None	6 mos.	Prob-able	Maintained	Slight	1 mo.	7 mos.	None	2 yrs., 4 mos.
18	L-1	24	Sports-woman	None	No defects	Almost complete	None	3 mos.	None	Maintained	Complete	.....	10 mos.	None	2 yrs.
19	L-3	36	Boatbuilder, C	Adolescent dorsal kyphosis; fracture of transverse process, L-1 and 3; ? lamina L-3	No defects	Almost complete	L-2 and 3	6 mos.	Yes	Maintained	Slight	5 mos. (over-seer)	Not yet to full activities	Dorsal pain intermittently	1 yr., 11 mos.
20	L-2	47	Steeple-jack, L†	Extensive fracture of both ankles L-2 articular process (?); old scoliosis	Old scoli-osis	Almost complete	None	4 mos.	Yes	Maintained	Upper ⅓, lower ⅓	None	None	Back "stiff," no pain, hallus rigidus	1 yr., 7 mos.
21	L-1, 2	49	R. R. freight conductor, C	Fracture of pelvis, transverse processes L-2 and 3	Partial sacraliza-tion L-5 transverse process	.....	None	None	None	None	Upper ⅓, lower com-plete	11 mos.	.....	None	1 yr.
22	D-12	46	Housewife	None	No defects	Almost complete	None	5½ mos.	.....	Maintained	About ½	.....	9 mos.	None	10 mos.

* In this column, C means that compensation was sought. L means lumbar, and D, dorsal.
† From date of injury.

TABLE 6.—*End-Results—Continued*

Case	Vertebra	Age	Occupation*	Complications	Lumbosacral Junction	Estimate of Correction	Surgical Fusion	Period of Fixation	Apparent Fusion by Bridging	Correction of Body	Estimated Loss of Intervertebral Space	Return to Light Activities†	Return to Preinjury Activities†	Symptoms; Nature of Disability	Time of End-Result
23	L-1	34	Tree surgeon's assistant, C	None	No defects	Almost complete	None	4 mos.	.....	Maintained	Upper ⅔, lower ½	.....	.....	None	9 mos.
24	L-2	15	Student	None	No defects	Almost complete	None	4 mos.	.....	Maintained	Upper ½, lower ¼	.....	7 mos.	None	8 mos.
25	L-1	52	Station fireman, C	None	Horizontal sacrum	No change	None	6 mos.	Yes	None	None	2½ mos.	9 mos.	None	2 yrs., 5 mos.
26	L-2	46	Porter, C	Fracture of pelvis, wrists and femur	Failure of fusion of 1st sacral neural arch	No change	None	7 mos.	Yes	None	Complete	8 mos.	13 mos.	Aches in muscles in lower part of back when tired	2 yrs.
27	L-1, 2	32	Milkman, C	Fracture of transverse processes L-1, 2 and 3	Failure of fusion of 1st sacral neural arch	Almost complete	L-1, 2 and 3	3 mos.	Yes	Maintained	About ½	.....	9 mos.	None	4 yrs., 7 mos.
28	D-11, 12	38	Scrubwoman, C	None	No defects	Partial correction	None	7½ mos.	None	Maintained	Complete	10 mos. (housework)	Has not tried	"Tires" in lower part of back, no pain	3 yrs., 10 mos.
29	D-12, L-1	18	Mechanic, L	Fracture of superior articular process and lamina L-1	Failure of fusion of 1st sacral neural arch	No change	None	2½ mos.	Yes	None	Complete	15 mos. (chauffeur)	Tried and failed	Pain in muscles in lower part of back on prolonged heavy labor	3 yrs., 7 mos.
30	D-11, 12	39	Chain store manager	None	No defects	Slight correction	D-11 and 12 and L-1	6 mos.	Unknown	Maintained	About ½	.....	14 mos.	None	2 yrs., 4 mos.
31	L-1, 2	40	Mechanic	Fracture of transverse process L-2, superior articular process (?)	No defects	Almost complete	None	3½ mos.	Yes	Maintained	About ½	.....	5 mos.	None	2 yrs., 3 mos.

* In this column, C means that compensation was sought. L means lumbar, and D, dorsal.
† From date of injury.

The nature of the adaptive changes indicates, however, an effort on the part of the tissues to establish an ankylosis at the site of injury which, as shown by roentgenogram, seems not infrequently to be successful. If such effort is uniformly and demonstrably inadequate, the need of help, as by spinal fusion, is indicated. Furthermore, the increase in the anteroposterior spinal curves resulting from the loss of the disk leaves a mechanical situation which is to some degree less sound and to which the patient must always accommodate himself in the future.

The results in these cases, at least over a period of from two to five years, lead one to believe that such practice is not indicated as a routine procedure. When permanence in an almost complete restoration of mechanics is desired, the procedure should be limited to fusing the corrected vertebra to its fellow opposite the disk whose narrowing is inevitable.

Operative spinal fusion following correction and before much narrowing of the disk occurred resulted in the permanence of most of the

TABLE 7.—*Data on Patients Who Have Not Returned to Preinjury Activities*

Case	Correction	Reason
2	Almost complete	Cannot find work
9	None attempted	Low backache
20	Almost complete	Painful hallux rigidus and fused ankles; is a steeplejack
23	Almost complete	Too early (9 months)
28	Partial	Because of litigation

intervertebral space in four cases in this series which would otherwise have been lost. In these cases the postreduction mechanics of the back have remained practically constant throughout two, four and four and a half years, respectively (figs. 5 and 9). Its practice should not unduly prolong the total convalescence, but recumbence will be considerably lengthened in cases otherwise suited to jacket and ambulatory care. Its advantages in preserving better mechanics must be weighed against the disadvantages of added cost, a period of hospitalization, the risk of operative intervention and the possible detriment to the patient's morale. I believe it was definitely indicated only in cases partially corrected in group 4 (the fracture-dislocation group), and possibly in group 3. In such cases, it should be practiced with the spine in extension and the fusion made to include that vertebra above whose superior surface is parallel with the inferior surface of the fractured vertebra, or the one below, if the inferior intervertebral space is narrowed (usually four in all). Six months should be allowed for the completion of the fusion. Intensive corrective exercises are then essential, if freedom from backache is to be assured. The deep lumbar lordosis, habitual after six months, must be eliminated, as in the case in which no fusion is performed.

SUMMARY

1. Recent fractures of the vertebral body can be corrected so as to reestablish preinjury mechanics of the back (96 per cent in this series).

2. Recent fracture and dislocation are more difficult of reduction (40 per cent in this series).

3. Part of this correction is usually lost (84 per cent in this series) through the ultimate gradual narrowing of the injured intervertebral disk.

4. The back is capable of a remarkable degree of adaptability to this change (65 per cent returned to preinjury activities in eight and a third months, as an average, and remained free from symptoms).

5. Reorganization or union of bone occurred in all cases, and is probably fully adequate in from two to seven months in most cases.

6. Correction may be lost through inadequate fixation.

7. The mechanics of correction through hyperextension are demonstrated.

8. The risk of injury to the cord through hyperextension is probably confined to cases of fracture and dislocation, and is probably not great, with care, in these.

9. Passing interruption of function of the cord occurred during hyperextension in one case of fracture and dislocation and manifested itself as a loss of reflexes and a motor paralysis of the lower extremities for several days.

10. Complete bridging of bone across the intervertebral region occurs in a large number of cases (42 per cent in this series) and may be apparent as early as four months and up to four and a half years.

11. Spinal fusion in extension is indicated in cases of fracture with dislocation when adequate correction cannot be obtained.

THE SCHILLING HEMOGRAM IN APPENDICITIS

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All clinicians agree that the diagnosis of appendicitis must rest on an interpretation of the clinical history and the physical signs rather than on a laboratory test. However, surgeons have often been impressed with the lack of correlation between the clinical manifestations of appendicitis and the observations at operation and the microscopic pathologic aspect of the appendix. Any laboratory test which aids in preoperative differentiation between inflammatory and noninflammatory conditions or which can serve as an index of the severity of the infection should prove of value.

It is desirable that the stage, severity and complications of appendicitis be determined as accurately as possible before operation. This is particularly important in clinics where the conservative (Ochsner) treatment is employed in selected cases. In this connection the history and physical signs are of foremost importance. The duration of symptoms, the change in the character, location or severity of the pain and the presence or absence of a mass or of generalized or localized tenderness, rigidity or rebound tenderness are all factors to be studied critically in forming an opinion regarding the pathologic process present and the plan of treatment to be pursued. The pulse rate and the temperature provide additional information as to the severity of the disease.

Widely divergent opinions have been expressed concerning the value of blood counts in the diagnosis of appendicitis. Disagreement is to be expected, as some authors have referred to the leukocyte count alone, others have included the Ehrlich [1] differential count, and recently more complete methods of examination of the blood film, such as the Schilling hemogram, have been investigated. There is no point in discussing the value of the leukocyte count alone. It is sufficient to mention that Finney [2] found a leukocyte count below 10,000 in only 8 per cent of a series of 1,162 patients including those with acute appendicitis and appendicitis with abscess or peritonitis.

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1. Ehrlich, L., quoted by Harter and Lyons.[7]

2. Finney, J. M. T., Jr.: Appendicitis: Some Observations Based on Review of Three Thousand, Nine Hundred and Thirteen Operative Cases, Surg., Gynec. & Obst. **56**:360, 1933.

The differential count now commonly used, which classifies cells into lymphocytes, monocytes, polymorphonuclears, eosinophils and basophils, was first formulated in 1891 by Ehrlich. In 1904 Arneth [3] discovered that the variations in the nuclear structure of the polymorphonuclear leukocytes can be correlated with the severity of the disease. He made an extensive classification of the neutrophils according to the number of lobes and their shape. In all there are more than eighty classes of leukocytes. This count was too complicated for routine clinical application, but it paved the way for further studies. In 1912 a satisfactory simplification of the Arneth index was devised by Victor Schilling.[4] He divided the neutrophils into four classes according to the state of immaturity of the nucleus. The four groups consist of: myelocytes; juvenile forms, which are the metamyelocytes of Pappenheim; stab or band forms having no definite nuclear lobulations, and mature segmented cells. Other modifications of the Arneth count have been originated by Cooke, Piney and Farley.

The surgical application of the Schilling hemogram has been the subject of recent papers by Yaguda,[5] Luck,[6] Harter and Lyons,[7] Goodale and Manning [8] and Fitz-Hugh,[9] who agreed essentially that the Schilling index is of more clinical value than the older Ehrlich method in detecting the presence, the degree and the persistence of infection.

It is not the purpose of this article to discuss the technic of making the Schilling count or its biologic significance, as these subjects have been covered by Schilling, Bredeck,[10] Yaguda and others. An excellent but brief review of the Arneth count, the Schilling hemogram and other modifications of the Arneth count is to be found in a recent contribution by Fitz-Hugh, who emphasized the limitations of these methods. It is sufficient to state here that the Schilling hemogram is a relatively simple means of recording the reaction of the bone marrow to infection or to toxic stimuli. In this count the lymphocytes, monocytes, eosinophils and

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3. Arneth, J., quoted by Schilling.[4]

4. Schilling, V.: The Blood Picture, St. Louis, C. V. Mosby Company, 1928.

5. Yaguda, A.: Studies on Schilling Count in Appendicitis, Am. J. Clin. Path. **1**:39, 1931.

6. Luck, J. V.: Schilling Differential Blood Count in Appendicitis, Am. J. Surg. **19**:275, 1933.

7. Harter, J. S., and Lyons, C.: Surgical Applications of the Schilling Differential Blood Count, Surg., Gynec. & Obst. **56**:182, 1933.

8. Goodale, R. H., and Manning, N. E.: The Schilling Index in Appendicitis, J. Lab. & Clin. Med. **16**:386, 1931.

9. Fitz-Hugh, T., Jr.: Present Day Modifications of the Arneth Count in Surgical Practice: A Clinical Review, Internat. S. Digest **15**:195, 1933.

10. Bredeck, J. F.: The Schilling Blood Differential Count in Tuberculosis, Am. Rev. Tuberc. **20**:52, 1929.

basophils are listed as in the Ehrlich differential count, but the neutrophils are further classified into segmented forms, stab cells, juvenile cells and myelocytes. In infectious diseases neutrophils enter the blood stream in earlier stages of development than normally, so that there is an increase in the number of stab cells and juvenile cells, and even myelocytes may appear, the presence of the latter indicating a severe infection. The increase in the number of nonsegmented neutrophils in the circulating blood is referred to as a shift to the left.

A standard normal Schilling hemogram may be found in tables 1 to 6, but it should be noted that variations may occur in normal persons. Fitz-Hugh said, "We consider the normal adult non-filament [11] count to be between four and ten per cent of the total leukocytes and would not be willing to draw any weighty deductions from a 'shift' of less than ten per cent magnitude."

In interpreting the blood picture the total leukocyte count, the percentage of neutrophils, lymphocytes, monocytes and eosinophils and the degree of shift to the left must all be given consideration. The total leukocyte count is generally believed to be an indication of the resistance of the body to infection. The percentage of neutrophils and the shift to the left correspond to the severity of the infection. The percentage of lymphocytes, monocytes and eosinophils decreases as the infection becomes more severe and increases as the infection subsides.

Yaguda, from a study of 671 cases in which the Schilling index was correlated with the histologic observations on the appendix, concluded (1) that the presence of a normal percentage of immature forms rules out a diagnosis of appendicitis; (2) that a count of immature cells of less than 14 per cent indicates a mild process, probably limited to the mucosa; (3) that a count of immature cells of more than 14 per cent indicates diffuse suppurative appendicitis of increasing severity as the count approaches 30 per cent; (4) that a count of immature forms of more than 35 per cent indicates perforation with peritonitis, and (5) that repeated counts are of definite prognostic value.

Although we were skeptical about the possibility of determining the exact pathologic process present by the degree of shift to the left, we undertook the study of the blood count on a series of 107 patients to estimate the value of the hemogram; as a means of differentiating between appendicitis and other conditions causing pain in the right lower quadrant; as a means of differentiating simple acute appendicitis from appendicitis complicated by abscess or peritonitis, and as a prognostic aid in serious conditions. In this investigation the patients were studied clinically by one of us (H. A. C.); all the blood studies were made by the other (L. W.).

11. Nonsegmented.

For purposes of comparison the patients were classified in five separate groups (tables 1 to 6). In group 1 (19 patients) were placed all those for whom the pathologist returned a diagnosis of inactive appendicitis. Most of the patients in this group had had recurrent attacks characteristic of appendicitis. One patient had no physical signs of appendicitis, but an interval appendectomy was performed on the advice of the referring physician. In 6 patients, tenderness in the right lower quadrant was the only physical sign. In 1 patient who had both cholecystectomy and appendectomy, it was found at operation that the symptoms had been due chiefly to hydrops of the gallbladder.

In group 2 (13 patients), in which the condition was designated as "mild appendicitis," were placed the patients who showed some slight change, such as peritonitis of the appendix, subacute appendicitis or mild acute appendicitis. It is recognized that there were some patients in this group for whom the diagnosis of appendicitis might be questioned. In others the condition undoubtedly represented the subsiding stage of acute suppurative appendicitis.

In group 3 (41 patients) were included all those with unquestioned acute suppurative appendicitis with no preoperative complications. The diagnosis was confirmed by operation and by microscopic examination of the appendix. In some of the patients in this group the appendix had patches of gangrene, and in some instances the peritoneal cavity contained clear or even turbid fluid, but none of the patients showed definite evidence of perforation or of peritonitis.

In group 4 (25 patients) were placed those who showed clinical evidence of local peritonitis or formation of an abscess. Conservative treatment was the rule in this group. However, all but 1 patient ultimately had either an appendectomy or drainage of an abscess.

In group 5 (9 patients) were included the patients with general peritonitis. One patient was operated on elsewhere seven days previous to admission to the University of Minnesota Hospital. She had diffuse peritonitis at the time of admission. Another patient had perforation at operation, with free pus in the peritoneal cavity. Operation was deferred in all the other cases. The only deaths in the entire series were the 3 which occurred in this group. The diagnosis of peritonitis complicating appendicitis was confirmed at necropsy in 2 of the 3 fatal cases, and in the third there was diffuse peritonitis, appendectomy having been performed elsewhere.

At least one Schilling count was made on each patient in the series. The count was usually made immediately on admission to the hospital. Repeated counts were made on some of the patients, particularly on those having abscess or peritonitis, so that the Schilling hemograms could be correlated with the clinical progress.

OBSERVATIONS

The age of the patient, the duration of symptoms, the temperature on admission, the pulse rate and the Schilling hemogram are tabulated (tables 1 to 6). Maximum, minimum and average values are given. The terms maximum and minimum refer to the highest and lowest values under each heading, not to the highest or lowest recorded for any one patient.

Group 1 (table 1).—The average leukocyte count, the average number of neutrophils and the average Schilling count in this group were all within normal limits. In only 6 of the 19 patients were the nonsegmented forms in excess of 10 per cent.

TABLE 1.—*Readings for Nineteen Patients in Group 1, with Inactive Appendicitis*

	Age, Years	Duration of Symptoms	Temperature, F.	Pulse Rate
Maximum	59	30 days	99.8	120
Minimum	12	10 hours	97.4	60
Average	29	5 days	98.6	85

		Schilling Hemogram								
	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
Standard	7 to 9,000	0 to 1	2 to 4	0	0 to 1	3 to 5	51 to 67	21 to 35	4 to 8	54 to 72
Maximum	13,600	1	12	1	5	21	76	51	2	80
Minimum	6,450	0	0	0	0	3	37	19	0	46
Average	9,576	0.05	2	0.05	1	8	60	27	0.5	70

The high leukocyte count with neutrophils and the shift to the left noted in some of the patients who had no demonstrable pathologic process in the appendix was probably due to the fact that the symptoms and signs were caused by some infectious process other than appendicitis. The Schilling count in this group was not always of value, because it could not be used to differentiate appendicitis from some other mild infection. However, it is worth while to notice that the shift to the left was usually slight if present. In some instances the Schilling hemogram was normal when leukocytosis was found to be present. Therefore the hemogram correlated more closely than the total white cell count with the appendical pathologic process. The following observations on 2 patients are examples:

Patient	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
I. F.	12,000	0	0	0	0	3	65	31	1	68
L. L.	13,600	0	1	0	1	5	74	19	0	80

Two patients in this group had eosinophilia. One, with 7 per cent eosinophils, had psoriasis, and the other, with 12 per cent eosinophils, vomited an ascaris following the appendectomy.

Group 2 (table 2).—The patients with mild appendicitis had average leukocyte counts and average neutrophil counts within the range of normal. The Schilling hemogram showed great variation, but the average count exceeded the upper limit of normal. Of the individual counts, 6 showed more than 10 per cent nonsegmented cells and 7, 10 or less. One patient in this group had a definite shift to the left, with 21 per cent stab and 6 per cent juvenile cells. This patient was reported to have peritonitis of the appendix. It is difficult to correlate the clinical and pathologic observations in this heterogeneous group, but it may be said that the pathologic evidence of appendicitis was not always conclusive and the changes in the blood picture were usually slight or absent.

Group 3 (table 3).—The correlation between the blood picture and the demonstrated pathologic changes was striking in this group of 41 patients with acute suppurative appendicitis. Thirty-eight had total leukocyte counts over 10,000, and 37 had more than 75 per cent of neutrophils. In 3 patients there were fewer than 10 per cent of nonsegmented neutrophils. Only 1 patient had a normal blood picture in the entire series of 41. This was a patient with subsiding appendicitis, the blood count having been made when the patient entered the hospital five days after the onset of symptoms.

TABLE 2.—*Readings for Thirteen Patients in Group 2 with Mild Appendicitis, Subacute Appendicitis and Peritonitis of the Appendix*

	Age, Years	Duration of Symptoms	Temperature, F.	Pulse Rate
Maximum	26	30 days	102.6	102
Minimum	9	6 hours	98.2	70
Average	17	5 days	99.2	93

		Schilling Hemogram								
	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
Standard	7 to 9,000	0 to 1	2 to 4	0	0 to 1	3 to 5	51 to 67	21 to 35	4 to 8	54 to 72
Maximum	13,950	4	4	0	6	21	76	46	2	85
Minimum	6,100	0	0	0	0	5	31	15	0	52
Average	9,385	0.4	0.9	0	2	10	58	28	0.8	70

TABLE 3.—*Readings for Forty-One Patients in Group 3 with Acute Suppurative Appendicitis*

	Age, Years	Duration of Symptoms	Temperature, F.	Pulse Rate
Maximum	70	14 days	103.0	135
Minimum	7	10 hours	98.0	60
Average	23	46 hours	99.6	95

		Schilling Hemogram								
	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
Standard	7 to 9,000	0 to 1	2 to 4	0	0 to 1	3 to 5	51 to 67	21 to 35	4 to 8	54 to 72
Maximum	24,000	1	2	3	5	31	77	48	3	95
Minimum	7,150	0	0	0	0	2	44	5	0	51
Average	15,310	0.02	0.2	0.3	2	17	63	16	0.5	83

The hemograms of 2 patients who had practically normal Schilling counts but an increase in the total number of leukocytes and some increase in the number of neutrophils are:

Patient	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
J. G.	10,300	0	0	0	0	7	69	21	3	76
L. S.	14,300	0	0	0	1	9	77	13	0	87

Even in these examples, including two of the three lowest counts for nonsegmented cells in group 3, the percentage of stab cells was increased above the normal standard.

The advantage of the Schilling count over the Ehrlich differential count is illustrated in the following case in which the leukocyte count and the percentage of lymphocytes and neutrophils were normal:

A. O. had acute suppurative appendicitis with bands of adhesions producing partial strangulation of the small intestine. The fluid in the peritoneal cavity showed streptococci and staphylococci on culture. The Schilling count was:

White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
8,450	0	0	0	2	22	44	32	0	68

In the case of O. S. the Schilling hemogram was of more significance than the white blood cell count or the percentage of neutrophils.

White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
10,000	0	2	2	6	21	51	18	3	77

The following count is an example of the unreliability of the leukocyte count alone. The patient, S. S., postoperatively became seriously ill with signs of peritonitis. The increased shift to the left was a much more accurate index of the clinical course. The patient recovered.

Date	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
4/28	13,250	0	0	0	4	15	74	7	0	93
Immediate operation on 4/28										
5/1	8,800	0	0	0	2	40	49	9	0	91

Experience with the Schilling hemogram in acute suppurative appendicitis indicates that a decided shift to the left may occur when the total leukocyte count and the total neutrophil count are normal. On the other hand, in some instances definite leukocytosis may be present when the Schilling count is not significantly altered. If a complete study of the blood is made, some alteration of the blood picture indicating the presence of infection will almost always be found in the active stage of acute suppurative appendicitis.

TABLE 4.—*Readings for Twenty-Five Patients in Group 4 with Appendicitis with Local Peritonitis or Abscess*

	Age, Years	Duration of Symptoms	Temperature, F.	Pulse Rate
Maximum	71	30 days	102.6	136
Minimum	7	20 hours	98.0	60
Average	37	6 days	100.5	100

		Schilling Hemogram								
	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
Standard	7 to 9,000	0 to 1	2 to 4	0	0 to 1	3 to 5	51 to 67	21 to 35	4 to 8	54 to 72
Maximum	29,050	1	2	4	5	44	81	40	2	95
Minimum	9,400	0	0	0	0	9	37	5	0	59
Average	17,456	0.04	0.2	0.4	2	20	60	13	0.6	86

Group 4 (table 4).—Great variations were noted in the leukocyte count, in the total number of neutrophils and in the degree of shift to the left in the patients of this group. This was to be expected, as the group included patients with various stages of local peritonitis and formation of abscesses. Only 2 patients had a leukocyte count of less than 10,000, and 4 had a normal percentage of neutrophils. Three had a Schilling hemogram showing less than 10 per cent of nonsegmented forms, but in these the duration of the disease varied from two weeks to more than a month.

Changes of the blood picture occurring in 1 patient (E. P.) as the clinical picture changed from that of local peritonitis to that of a walled-off appendical abscess are illustrated.

Date	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
6/29	11,000	0	0	0	1	34	58	7	0	93
7/ 1	6,550	0	0	1	2	47	39	10	1	89
7/ 5	10,600	0	0	3	4	33	48	12	0	88
7/ 9	11,150	0	0	0	0	20	62	17	1	82
7/12	7,300	0	0	0	0	6	55	36	3	61

The abscess was drained on July 13, one day after the last examination of the blood.

The two hemograms which were taken on 1 patient (F. S.), one on his first admission to the hospital when he had an appendical abscess and the other a month later when he returned for appendectomy, were as follows:

Date	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
3/6	11,900	0	1	4	4	26	37	28	0	71
4/4	6,800	0	0	0	0	10	61	28	1	71

The white cell count was elevated in the first instance, but if an Ehrlich differential count had been done a mild infection would have been indicated. In this case the Schilling count was a much more accurate index of the severity of the patient's condition.

The great variations noted in this group confirm rather than oppose the idea that a shift to the left is related to the severity of the infection, as it was only in old subsiding conditions that normal counts were obtained. The counts showing the highest number of nonsegmented neutrophils were invariably in patients in the acute stage of local peritonitis or formation of an abscess. Some of the abscesses were drained subsequently. Some patients had appendectomies after several weeks of conservative treatment, and usually at operation there were numerous adhesions indicating previous peritonitis.

TABLE 5.—*Readings for Nine Patients in Group 5 with Appendicitis with Diffuse Peritonitis*

	Age, Years	Duration of Symptoms	Temperature, F.	Pulse Rate
Maximum	50	10 days	102.4	140
Minimum	5	56 hours	98.0	92
Average	25	5 days	100.9	117

		Schilling Hemogram								
	White Blood Cells	Baso-phils	Eosino-phils	Myelo-cytes	Juve-niles	Stab Cells	Seg-mented Cells	Lym-pho-cytes	Mono-cytes	Total Poly-morpho-nuclears
Standard	7 to 9,000	0 to 1	2 to 4	0	0 to 1	3 to 5	51 to 67	21 to 35	4 to 8	54 to 72
Maximum	37,800	0	1	3	7	55	73	24	5	95
Minimum	5,450	0	0	0	2	23	15	5	0	76
Average	14,950	0	0.1	0.9	4	40	44	10	0.7	89

Group 5 (table 5).—The Schilling counts on the 9 patients with diffuse peritonitis showed a marked shift to the left, although in some instances the total number of leukocytes was normal. In this group the blood picture invariably indicated a severe infection at some period of observation.

For example, L. S. had an appendectomy performed elsewhere seven days prior to admission to the hospital. On admission there were signs of diffuse peritonitis. The patient died the following day. The blood count was:

White Blood Cells	Basophils	Eosinophils	Myelocytes	Juveniles	Stab Cells	Segmented Cells	Lymphocytes	Monocytes	Total Polymorphonuclears
6,000	0	0	2	4	55	15	24	0	76

Another hemogram is given to show the changes occurring in the blood of a man (J. L.) operated on for acute appendicitis with early perforation and peritonitis. After operation he showed signs of diffuse peritonitis, but he ultimately recovered. The hemograms were:

Date	White Blood Cells	Basophils	Eosinophils	Myelocytes	Juveniles	Stab Cells	Segmented Cells	Lymphocytes	Monocytes	Total Polymorphonuclears
7/27	15,650	0	0	0	4	23	68	5	0	95
8/ 3	7,550	0	0	0	4	47	29	20	0	80
8/12	13,300	0	0	1	0	24	61	14	0	86
8/21	7,900	0	0	0	1	12	66	19	0	81

Three deaths occurred in this group. The hemograms showed a marked shift to the left, but no difference could be detected between the counts on those who survived and those who died. The series of counts for E. C. shows that survival may occur, even when the Schilling hemogram indicates a bad prognosis.

E. C., aged 39 years, was admitted on June 21, 1933, with a history suggesting appendicitis with perforation of the appendix. The clinical picture was that of diffuse peritonitis. The patient was treated conservatively. On July 5 and September 5 pelvic abscesses were drained. The hemograms were:

Date	White Blood Cells	Basophils	Eosinophils	Myelocytes	Juveniles	Stab Cells	Segmented Cells	Lymphocytes	Monocytes	Total Polymorphonuclears
6/22	5,450	0	0	0	4	47	37	12	0	88
6/23	4,850	0	0	3	6	47	29	15	0	85
6/27	13,150	0	1	0	4	31	51	13	0	86
6/30	14,100	0	1	0	6	45	36	12	0	87
7/ 3	13,250	0	0	1	7	53	27	12	0	88
7/ 7	11,200	0	1	0	5	29	48	17	0	82
7/12	9,350	0	1	0	2	12	61	22	2	75
7/17	19,000	0	0	0	4	20	63	13	0	87
7/31	9,750	0	0	0	1	34	48	17	0	83
8/12	12,000	0	0	0	4	33	40	23	0	77
8/19	9,150	0	2	0	3	20	42	33	0	65

The patient was dismissed from the hospital much improved after drainage of the two abscesses.

TABLE 6.—*Comparison of the Averages of Schilling Count, Pulse Rate and Temperature of the Five Groups*

	White Blood Cells	Basophils	Eosinophils	Myelocytes	Juveniles	Stab Cells	Segmented Cells	Lymphocytes	Monocytes	Total Polymorphonuclears	Temperature, F.	Pulse Rate
Standard	7 to 9,000	0 to 1	2 to 4	0	0 to 1	3 to 5	51 to 67	21 to 35	2 to 4	54 to 72	98.6	80
Group 1	9,576	0.05	2.0	0.05	1	8	60	27	0.5	70	98.6	85
Group 2	9,385	0.4	0.9	0.0	2	10	58	28	0.8	70	99.2	98
Group 3	15,310	0.02	0.2	0.3	2	17	63	16	0.5	83	99.6	95
Group 4	17,458	0.04	0.2	0.4	2	20	60	13	0.6	86	100.5	100
Group 5	14,950	0.0	0.1	0.9	4	40	44	10	0.7	89	100.9	117

TABLE 7.—*Temperature on Admission to the Hospital*

	Group 1, 19 Patients	Group 2, 13 Patients	Group 3, 41 Patients	Group 4, 25 Patients	Group 5, 9 Patients
99 F. or under	14	10	14	5	1
99.1 to 100 F.	5	1	15	6	0
100.1 to 101 F.	0	1	10	4	3
101.1 to 102 F.	0	1	1	8	3
102.1 to 103 F.	0	0	1	2	2

TABLE 8.—*Pulse Rate on Admission to the Hospital*

	Group 1, 19 Patients	Group 2, 13 Patients	Group 3, 41 Patients	Group 4, 25 Patients	Group 5, 9 Patients
80 or less	7	1	10	1	0
81 to 100	10	10	19	13	4
101 to 120	2	2	8	9	1
121 to 140	0	0	4	2	4

COMMENT AND SUMMARY

In this study we found an increase of the average shift to the left for each succeeding group of patients, beginning with the patients with an inactive appendix and ending with those with acute appendicitis and diffuse peritonitis. Variations of the blood picture occurred within each group, but in a general way they corresponded with the clinical variations which also occurred within each group; that is, when the appendicitis was clinically mild or subsiding the blood counts approached more nearly the normal and when the disease was active and more severe greater shifts from the normal occurred. We do not propose to attempt to diagnose appendicitis or to differentiate its stages or gage its severity entirely on the number or percentage of any type of blood cell, but we believe that when considered with the history, physical signs, temperature and pulse rate, the Schilling differential blood count is of real value in differentiating between inflammatory and noninflammatory conditions and in estimating the severity of the disease. In this respect it is decidedly of more value than the leukocyte count alone, and it is also of more value than the Ehrlich differential count.

In tables 1 to 6 are given the maximum, minimum and average temperature and pulse rate (recorded on admission to the hospital for comparison with the hemogram). In tables 7 and 8 is given more detailed information regarding the temperature and pulse rate of the patients in the various groups. Both the temperature and the pulse rate showed great variation, and the temperature especially was unreliable in providing evidence of the presence of infection or in enabling one to judge the seriousness of the infection present. The pulse rate appeared to be a slightly better index of the severity of the infection but as 29 of 41 patients in group 3, 14 of 25 patients in group 4 and 4 of 9 patients in group 5 had a pulse rate of 100 or less, and as some patients in each

of the three groups had a pulse rate over 120, the pulse rate cannot be called a delicate test of the severity of the infection. It is our opinion that the Schilling hemogram is of greater independent value than either the temperature or the pulse rate in estimating the severity of the infection present.

CONCLUSIONS

The Schilling hemogram is superior to the total leukocyte count and to the Ehrlich differential count in estimating the presence or severity of infection.

In appendicitis the Schilling hemogram is a better index of the severity of the disease than either the temperature or the pulse rate.

A marked shift to the left may indicate a bad prognosis, but not necessarily a fatal one. Some patients who survived showed greater shifts than others who died.

In clinics where conservative treatment is employed in appendicitis with perforation or in subsiding appendicitis, the Schilling hemogram should be an aid in determining the stage and severity of the disease and in following its progress.

RELATION OF ARTERIES TO ROOTS OF NERVES IN POSTERIOR CRANIAL FOSSA IN MAN

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The removal of a portion of the occipital bone has become a well established and frequently used surgical method of approach in operations on certain of the cranial nerves. The posterior cranial fossa is opened on the side indicated, and the roots of the nerves may be identified as they pass from the brain toward their exit through the dura mater and the cranial foramina.

The sensory root of the trigeminal nerve may thus be exposed and sectioned for the relief of tic douloureux. For a similar intense glossopharyngeal neuralgia, the ninth cranial nerve may be reached and cut. By the same route the vestibular portion of the acoustic nerve has been divided to provide relief from the intolerable vertigo of Ménière's disease.

In all of these procedures surgeons have encountered certain hazards and complications which have added considerably to the difficulty of performing the operation successfully. One of the most serious dangers is that of hemorrhage due to the cutting or the injuring of a blood vessel which may lie either on the nerve to be sectioned or in close proximity to it.

Arteries not described in the ordinary textbook of anatomy are sometimes encountered lying on the nerves which are to be divided. In other cases large arterial trunks may exhibit flexures which bring them into the field of an operation in which they are not usually present. Here they may provide obstructions which prevent the surgeon from obtaining a clear route to the structure he wishes to reach, and they are in serious danger of being wounded. They may, of course, be ligatured or clipped, but no surgeon voluntarily disposes of them in this manner, as he may immediately precipitate serious symptoms by the deprivation of a part of the brain of its blood supply. In saving the artery from injury, he may encounter considerable added difficulty in performing the operation successfully.

Recognizing the conditions just enumerated, we undertook an investigation of the variations of the arteries lying in the posterior cranial fossa. Extensive work has been accomplished, the results of which

are later to be published in full. It was thought desirable, however, to report in a separate paper the facts referring to the relation of the arteries and the nerve roots which we had obtained, since this information is of special value to the neurologic surgeon.

The observations recorded in the present paper are the results of the study in approximately sixty cases of the arteries supplying the hindbrain. Thirty-five brains were obtained from bodies in the dissecting room; the rest were secured at autopsy and were immediately preserved in a dilute solution of formaldehyde. The material used was in good condition. Since records were made only of the vessels which could be followed definitely and accurately, a complete record of all of the arteries of each brain was not made.

We observed, as has been previously noted by many other workers, that the right and the left vertebral artery were frequently unequal in size and unsymmetrical in course. The level of their union to form the basilar artery varied considerably, from the normal position at the lower limit of the pons to one a few millimeters above or 1.5 cm. below this location. The length of the basilar artery thus varied considerably. Variations also appeared in its course; it was sometimes curved or tortuous to a marked degree and was displaced from the median line. All of these changes have been frequently noted before. As they are not of such immediate clinical application to surgical procedures with nerve roots as are the other observations reported in this paper, no detailed description of them will be given here.

INVESTIGATIONS

The relation of the blood vessels to the roots of the cranial nerves in the posterior cranial fossa is reviewed in the order of the occurrence of the nerves, beginning with the fifth or trigeminal nerve.

Trigeminal Nerve.—A constant branch arising from the anterior part of the basilar artery was observed coursing transversely across the pons and passing to the ventral surface of the sensory root of the trigeminal nerve. This vessel (figs. 4, 6, 7, 8, 9 and 10) was sometimes of considerable size. Stopford[1] also noted it in many of his preparations. Being situated ventral to the nerve root, it is sheltered and is not visible to the surgeon. Thus it is in danger of being divided with the nerve in an operation for the relief of tic douloureux, which involves the division of the entire sensory root of the fifth nerve. This artery apparently supplies the nerve root and the semilunar ganglion. The vessel is not mentioned in the textbooks; we therefore suggest the term "trigeminal artery."

1. Stopford, J. S. B.: The Arteries of the Pons and Medulla Oblongata, J. Anat. & Physiol. **50**:131 and 255, 1915-1916.

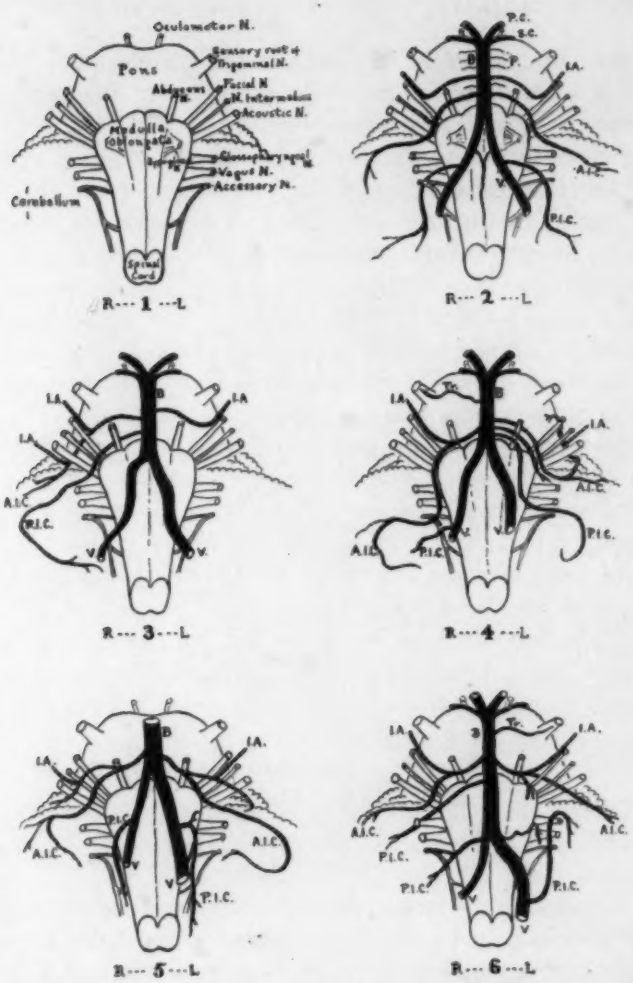

Fig. 1.—Key sketch showing inferior surface of cerebellum, pons and medulla oblongata with roots of third to twelfth cranial nerves.

Fig. 2.—Idealized scheme of vertebral and basilar arteries and their branches, based on textbook descriptions. Arterial branches are equal and symmetrical; internal auditory artery is shown arising on basilar; anterior inferior cerebellar artery crosses ventral to roots of abducens, facial and acoustic nerves, and posterior inferior cerebellar artery, on its way to cerebellum, passes ventral to roots of glossopharyngeal, vagus and accessory nerves or through interval between latter two. In this diagram and in figures 3 to 10, *R* denotes the right side and *L*, left side. Arteries are designated as follows: *A.I.C.* is anterior inferior cerebellar; *B.*, basilar; *I.A.*, internal auditory; *P.*, pontile; *P.C.*, posterior cerebral; *P.I.C.*, posterior inferior cerebellar; *S.C.*, superior cerebellar; *Tr.*, trigeminal, and *V.*, vertebral.

Figs. 3 to 10.—Arterial relations noted in cases studied. Diagrams illustrate all possible positions of internal auditory, anterior inferior cerebellar and posterior inferior cerebellar arteries. Trigeminal artery is shown in several instances. Complete descriptions of these arteries and their relations to nerve roots are contained in the text.

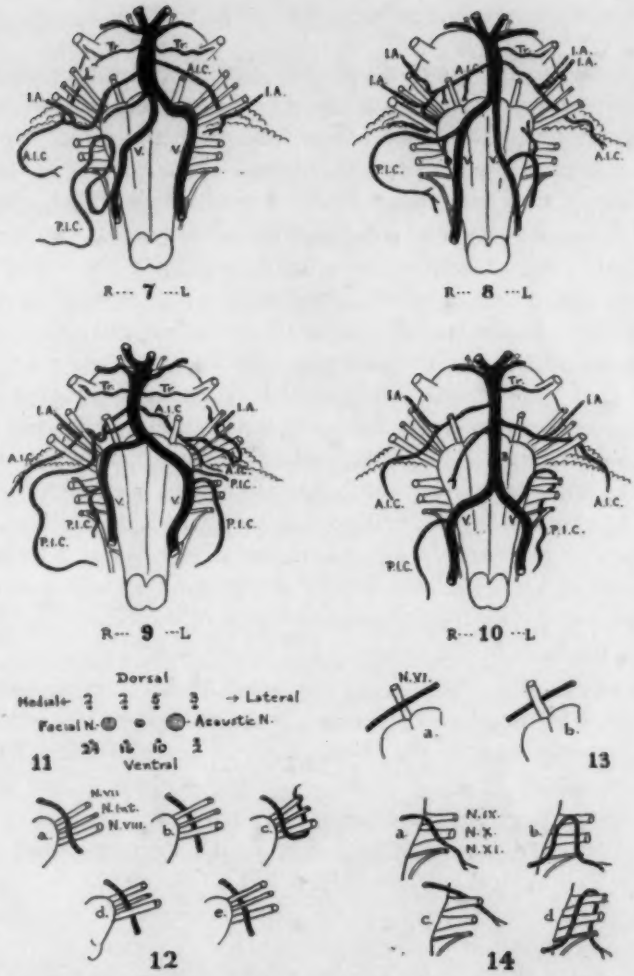

Fig. 11.—Eight positions relative to roots of facial, intermediate and acoustic nerves which may be assumed by internal auditory artery in its course to internal auditory meatus. Numerals indicate relative frequency of each position as noted in sixty-four cases.

Fig. 12.—Relation of anterior inferior cerebellar artery to roots of facial, intermediate and acoustic nerves. Artery may run ventral to (*a*), dorsal to (*b*) or in loop about (*c*) nerve roots; it may pass from ventral to dorsal surface between intermediate and acoustic nerves (*d*), or from dorsal to ventral surface in between intermediate and acoustic nerves (*e*).

Fig. 13.—Relations of anterior inferior cerebellar artery to root of abducens nerve. In *a*, artery lies ventral to nerve; in *b*, dorsal.

Fig. 14.—Relations of posterior inferior cerebellar artery to roots of glossopharyngeal, vagus and accessory nerves. Artery passes: in *a*, from a high origin to cerebellum ventral to nerve roots; in *b*, from a low origin in a loop ventral to nerve roots; in *c*, from a high origin superior to glossopharyngeal nerve, crossing it on way to cerebellum, and in *d* from a low origin, as a loop on way to cerebellum in concavity of which nerve roots are contained. In either of last two positions artery may press on ninth nerve and be in danger during operation on this nerve.

Just dorsal to the nerve root, and often as well somewhat lateral to it, is a vein which passes from the superior surface of the cerebellum to the superior petrosal sinus. This vein is in the direct route of the surgeon, and prevents perfectly free access to the root of the nerve.

Recently a case has come to our notice which ended fatally after section of the sensory root of the trigeminal nerve. At operation a sudden hemorrhage occurred immediately following the avulsion of the nerve root with a blunt hook. The bleeding was hard to control, but the wound was finally closed. Signs of increasing intracranial pressure gradually developed, and the patient died in the course of a few days, in spite of the remedial measures, which included a second operation revealing an extensive blood clot surrounding the medulla and pons.

The postmortem examination led to the conclusion that the main stem of the anterior inferior cerebellar artery had been torn, presumably because it possessed an unusually large loop which had allowed it to be picked up with the nerve. The main stem of the artery was filled with a solid clot and was separated from its origin on the basilar artery. The vessel was also embedded for some distance in the large clot which had formed at the base of the brain.

Abducens Nerve.—Section of this nerve is never indicated, since it is made up wholly of motor fibers. It lies very near the midline and is crossed by the main trunk of the anterior inferior cerebellar artery. In most cases this crossing lies close to the surface of the brain, but sometimes the artery is rather tortuous and forms a loop which extends farther out on the nerve. The artery may lie either dorsal to (figs. 4*L* and 8*R*) or ventral to (figs. 4*R*, 5 and 6) the nerve.

When the artery lies dorsal to the nerve it may exert pressure. Both Cushing [2] and Stopford [1] have suggested this as a cause of paralysis of the sixth nerve. In one case we found the nerve situated in a tight loop (fig. 9*L*) formed by the tortuous crossing of the anterior and the posterior inferior cerebellar artery just lateral to the nerve. Such a relation, it seems, might easily result as Stopford has suggested.

We observed that the dorsal position of the artery was encountered in twenty-four cases and the ventral position in forty-seven. These figures give a much higher proportion of cases with the artery in the dorsal position than those cited by Stopford, who noted this arrangement on the right side in 14 per cent of his cases and on the left in 19 per cent.

Facial, Intermediate and Acoustic Nerves.—Since the roots of these three nerves arise close to each other and all of them pass out together to enter the internal auditory meatus, their relations to the blood vessels are considered as a unit.

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2. Cushing, Harvey: Strangulation of the Nervi Abducentes by Lateral Branches of the Basilar Arteries in Cases of Brain Tumours, Brain **33**:204, 1910.

The artery which is constantly associated with this group of nerve roots is the internal auditory. The artery supplies not only the nerve roots but the sense organs of the internal ear, namely, the cochlea, the saccule, the utricle and the semicircular canals. It is therefore extremely important that the artery should not be wounded.

Its protection would be easily insured if it were as constant in position as one is led to believe from the descriptions in the various textbooks. It is described as coursing medially to the facial nerve and therefore in a safe location, since the only nerve section performed on this group of roots is that of the more lateral half of the acoustic nerve, which contains the fibers of the vestibular portion.

As a matter of fact, the internal auditory artery is extremely variable in its position, and in some of these locations it is in distinct danger. We have noted it passing in company with the nerve roots to the internal auditory meatus in eight distinct positions (fig. 11), which may be listed as follows:

A. Ventral positions
   1. Medial to the facial nerve (figs. 3 *L*, 4 *R*, 6 *R*, 8 *L* and 10 *R*)
   2. Between the facial and the intermediate nerve (figs. 5 *L* and 10 *L*)
   3. Between the intermediate and the acoustic nerves (figs. 5 *R* and 8 *R*)
   4. Lateral to the acoustic nerve (fig. 7 *R*)

B. Dorsal positions
   5. Medial to the facial nerve (figs. 3 *R* and 6 *L*)
   6. Between the facial and the intermediate nerve (figs. 9 *R* and 9 *L*)
   7. Between the intermediate and the acoustic nerve (fig. 4 *L*)
   8. Lateral to the acoustic nerve (figs. 3 *R* and 7 *L*)

It is to be noted that in the positions dorsolateral and ventrolateral to the acoustic nerve the artery lies directly on that part of the nerve which the surgeon wishes to cut. The artery is therefore placed in danger, and the difficulty of the operation considerably increased. In five of a total of sixty-four cases, the internal auditory artery was observed to be situated in such a position of danger (fig. 11).

We also found that in six of the cases the internal auditory artery was double (figs. 3*R*, 8*R* and 8*L*). In these instances one vessel was usually related to the facial and the other to the acoustic nerve.

The origin of the internal auditory artery is of special interest. The textbooks describe this vessel as a separate and independent branch of the basilar artery (fig. 2). In Italy this seems to be the more common origin, as appears in the work of Cavatorti,[3] who found that the artery arose in this manner on the right side in 70 per cent of his cases and on the left in 67 per cent. Working in two such widely separated regions

3. Cavatorti, P.: Il tipo normale e le variazioni delle arterie della base dell'encefalo nell'uomo, Monitore zool. ital. **19**:248, 1908; abstr., Jahresb. ü. d. Fortschr. d. Anat. u. Entwcklngsgesch. **14**:296, 1908.

as England and Japan, however, Stopford [1] and Adachi [4] noted independently that in the great majority of cases the internal auditory artery is a branch of the anterior inferior cerebellar artery and is given off as the latter vessel crosses the region of origin of the facial and of the acoustic nerve. In this investigation we found only three cases in which the internal auditory artery arose independently from the basilar (fig. 3*L*). In all of the other cases it was a branch of the anterior inferior cerebellar artery (figs. 3 to 10).

We also noted that the main trunk of the anterior inferior cerebellar artery was in constant relation to the roots of the facial, the intermediate and the acoustic nerve. The artery is a branch of the basilar artery; it courses over the pons and passes the roots of the three nerves just mentioned to gain the under surface of the cerebellum. The vessel may lie in contact with either the dorsal (figs. 3 *R* and 9 *R*) or the ventral (figs. 4, 5, 6 *R*, 7 *R* and 10 *R*) surface of the nerves; it gives off the internal auditory artery in one of the positions previously listed in the description of that vessel.

The anterior inferior cerebellar artery usually lies close to the surface of the brain and so does not interfere with the operation of dividing the vestibular part of the acoustic nerve. This is not always true, however, since the trunk of the artery sometimes lies far out from the brain on the nerve roots. Instances were seen also in which the artery rose in a loop (figs. 4 *L* and 7 *R*) some distance out on the nerve roots as it passed them. In a few cases the loop extended out far enough to come into contact with the petrous bone. In this position the vessel presents a distinct hazard, and, since it is of considerable size and supplies a large portion of the cerebellum, its injury, with the consequent application of ligatures or clips, is definitely to be avoided.

We have seen this vessel pass from the ventral to the dorsal surface of the nerves to which it is related by passing through the interval between the facial and the intermediate nerve (fig. 9 *L*) or in a similar manner between the intermediate and the acoustic nerve (figs. 8 and 10 *L*). Sometimes the passage is made in the reverse direction, that is, from the dorsal to the ventral surface through the same intervals (fig. 6 *L*).

In the cases in which the anterior inferior cerebellar artery passes between the nerve roots of the intermediate and the acoustic nerve it is held firmly in position and is difficult to move aside. This passage is sometimes made far from the brain surface, close to the mouth of the internal auditory meatus, and thus in the region in which the surgeon divides the vestibular nerve.

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4. Adachi, B.: Das Arteriensystem der Japaner, Kyoto, 1928, vol. 1, p. 119.

In conversation with Dr. Kenneth G. McKenzie, we learned that he has met cases similar to those cited and that they were a source of bewilderment, since he could find in the textbooks no mention of a large vessel the position of which corresponded to that seen at operation.

Glossopharyngeal, Vagus and Accessory Nerves.—These three nerves arise from an almost continuous series of rootlets emerging from the anterolateral surface of the medulla oblongata. After the addition of the spinal root to the accessory nerve, the nerves pass through the jugular foramen. The glossopharyngeal nerve lies anteromedial to the others and passes separately through the dura mater.

Only on the glossopharyngeal nerve, which he divides close to the jugular foramen, does the surgeon operate intracranially for the relief of such conditions as tic douloureux. The vessels, therefore, the relationships of which are of practical interest here are those connected with the ninth or glossopharyngeal nerve.

The posterior inferior cerebellar artery chiefly holds this relation. It arises in the great majority of cases from the vertebral artery (figs. 7, 8 and 10), but sometimes from the basilar (figs. 3 *R*, 4 *L*, 6 *R* and 9 R). It often forms a loop with the convexity forward (figs. 5, 7 *R*, 8 *L* and 9 *L*), and it comes in contact with the ventral surface of the rootlets of the glossopharyngeal, vagus and accessory nerves on its return to the under surface of the cerebellum. It usually lies close to the medulla, and frequently fails to extend as far forward as the glossopharyngeal nerve. In all such instances the vessel is not in danger. The textbooks state that it passes through the interval between the vagus and the accessory nerve to reach the cerebellum (fig. 4 *L*). In only three of the fifteen cases in which the artery occurred in the ventral position did we have the vessel passing through the interval between these nerves. In no case did the artery pass through the interval between the glossopharyngeal and the vagus nerve.

Other cases were noted, however, in which the artery arose farther forward than usual (fig. 9 *L*) or the loop extended well forward (fig. 7 *R*), so that the vessel extended farther laterally under the nerve and might therefore be cut in section of the latter.

A position invoking a greater hazard is that in which the artery arises high on the vertebral or occasionally on the basilar artery and crosses superiorly (or dorsally) to the nerve on its way to the cerebellum (figs. 6 *R* and 8 *R*). Viewed from above, the nerve and the artery appear, in crossing each other, to form a figure like the letter X, with the vessel superior and therefore in considerable danger in cases in which the glossopharyngeal nerve is to be divided.

The position of greatest danger to the vessel is one seen occasionally (figs. 6 *L* and 10 *L*) in which the posterior inferior cerebellar artery arises from the vertebral artery ventral to the nerve roots and then

runs superiorly to form a loop about the glossopharyngeal nerve. The artery then passes in the opposite direction to course on the surface of the cerebellum. The glossopharyngeal nerve is thus contained within the concavity of a loop formed by the artery. The vagus and the accessory nerve also, of course, lie within this loop. With the artery arching over the nerve in this fashion, access to the nerve for the purpose of cutting it is rather difficult. Pressure of an arterial loop such as that just described on the ninth nerve may well be the cause of severe glossopharyngeal neuralgia, as surgeons have suggested.

Hypoglossal Nerve.—This nerve is purely motor, and therefore intracranial section is not indicated. In this location it is also rather difficult of access. The vertebral artery lies inferior and anteromedial to the origin of the nerve. The posterior inferior cerebellar artery may course anterior to (on the ventral surface of) the nerve if the vessel arises high on the vertebral artery. This is of no practical significance.

Comment.—In conclusion, we wish to emphasize the extreme variability both of the origin and of the course of the arteries in the posterior cranial fossa. The descriptions of these vessels found in standard textbooks of anatomy are wholly inadequate and of little aid to the surgeon in providing definite, detailed information on which to base his surgical technic. We are at present preparing a full anatomic description of the vessels in the region which we have studied; this is to be published later.

SUMMARY

Those arteries of the posterior cranial fossa which have definite relations to the nerve roots have been described.

Emphasis has been laid on the practical application of these relations to operations on the nerve roots.

An almost constant branch of the basilar artery runs laterally across the pons to pass out on the ventral surface of the sensory root of the trigeminal nerve. The term "trigeminal artery" is suggested for this vessel.

The main trunk of the anterior inferior cerebellar artery shows many and varied relations to the roots of the facial, intermediate and acoustic nerves. It lies either dorsal to or ventral to the nerve roots; it may loop around them or may pass between any two of them.

In the vast majority of cases the internal auditory artery arises from the anterior inferior cerebellar artery and not from the basilar artery, as is stated in the textbooks.

The internal auditory artery may occupy many positions as it emerges with the nerves. It may be either dorsal or ventral to them, between any two of them, medial to the facial nerve or lateral to the acoustic nerve.

The posterior inferior cerebellar artery is in relation to the glossopharyngeal, the vagus and the accessory nerve. It may be ventral or dorsal to them, cross superiorly to the glossopharyngeal nerve or form a loop over that nerve. It may pass between the vagus and the accessory nerve.

Diagrams illustrating all of the positions already mentioned are included.

In the series of cases which we have reviewed, nearly all of the possible positions of the arteries were noted, and we have elaborated on them with special reference to their relations to the nerve roots and to the practical application of this knowledge by the surgeon.

ACUTE APPENDICITIS IN CHILDREN

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The diagnosis of acute appendicitis in children is frequently difficult because of the handicaps encountered in obtaining an accurate history and in performing an adequate physical examination. These difficulties may lead to the impression that there is a fundamental difference in the disease in children and in adults. The problem has been analyzed with reference to incidence, bacteriology, etiology, symptomatology, subjective and objective signs, mortality and factors influencing mortality in children in order to determine any differences there may be in the manifestations of acute appendicitis in children and in adults.

The records of 258 patients under 15 years of age admitted to the University of Virginia Hospital from 1925 to 1932, inclusive, which were filed under the diagnosis of "acute appendicitis" were reviewed. For purposes of comparison, certain figures have been drawn from a statistical study of the series of cases of acute appendicitis in adults, seen in this clinic during the same period.

INCIDENCE

The age, race and sex distribution for this series of cases are shown in table 1. No cases were encountered in children under 2 years of age. This emphasizes the fact that this condition is rare in infants. Abt,[1] in 1917, was able to find reports of only 80 cases of acute appendicitis in children under 2 years of age.

The incidence in this series rose gradually between the third and twelfth years. After this time there was a marked increase in the number of cases, the incidence in each of the last three years (thirteenth to fifteenth, inclusive) being fairly constant. In a series of 208 cases of acute appendicitis in children under 14 years of age studied by Richter,[2] the peak of the age distribution curve was noted in the tenth year, and there was a decided decline in the incidence in the succeeding

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From the Department of Surgery and Gynecology, University of Virginia School of Medicine.

1. Abt, I. A.: Appendicitis in Infants, Arch. Pediat. **34**:641 (Sept.) 1917.

2. Richter, H. M., in Abt, Isaac A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 3, p. 560.

years. In the series of cases from the St. Louis Children's Hospital (325 cases) reported by Keyes,[3] the peak was reached at the twelfth year, and was succeeded by a gradual decrease. The age distribution in these three series of cases suggests that in a large series the increase in incidence would be gradual, with no sharp rise at any age period during childhood.

In the present series of 258 cases, 55 per cent were in boys and 45 per cent in girls. This difference is not significant in this relatively small series, yet it is suggestive of the greater incidence in boys reported by other observers,[4] and of the greater incidence in men.[5]

TABLE 1.—*Distribution of Cases According to Age, Race and Sex*

	White		Negro		Total		
Age	Boys	Girls	Boys	Girls	Boys	Girls	Deaths
1	0	0	0	0	0	0	0
2	3	3	0	0	3	3	1
3	3	3	0	1	3	4	0
4	2	1	0	0	2	1	0
5	6	3	0	1	6	4	1
6	8	4	1	0	9	4	1
7	10	4	0	0	10	4	2
8	10	5	1	0	11	5	1
9	8	6	3	4	11	10	1
10	8	9	2	1	10	10	4
11	10	6	5	0	15	6	2
12	11	26	3	6	14	32	3
13	18	13	3	3	21	16	2
14	23	16	4	1	27	17	2
Total	120	99	22	17	142	116	20
Per cent					55	45	

In this series there were 219 white and 39 Negro children. These figures probably do not indicate the true ratio of acute appendicitis in white and in Negro children, though they approximate those given by Maes, Boyce and McFetridge.[4c]

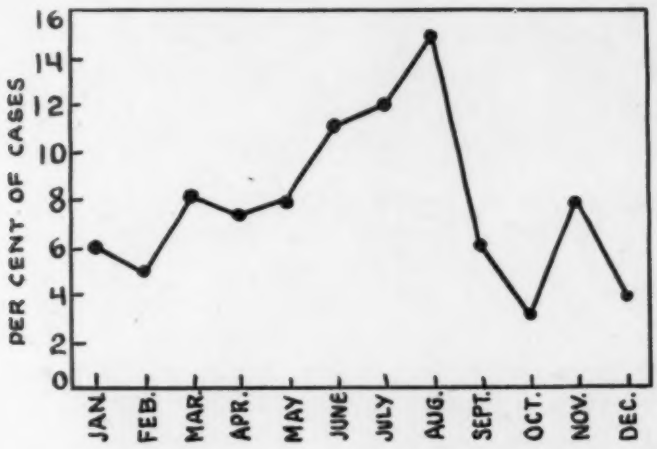
The seasonal incidence is shown in table 2 and in the chart. It is interesting that the peak of the curve of incidence of acute appendicitis comes in June, July and August. That the greatest incidence occurs

3. Keyes, E. L.: Death from Appendicitis, Ann. Surg. **99**:47 (Jan.) 1934.

4. (*a*) Richter.[3] (*b*) Alexander, E. G., and Deaver, J. B., quoted by Richter.[3] (*c*) Maes, U.; Boyce, F. F., and McFetridge, E. M.: Acute Appendicitis in Childhood, with a Critical Analysis of 250 Cases, Surg., Gynec. & Obst. **58**:32 (Jan.) 1934.

5. Keyes, E. L.: Death from Appendicitis, Ann. Surg. **99**:47 (Jan.) 1934. Finney, J. M. T., Jr.: Appendicitis, Surg., Gynec. & Obst. **61**:360 (Feb.) 1933.

in those months when intestinal infections are most common suggests a close relationship between such conditions and acute appendicitis. The absence of an increase in the number of cases of appendicitis during the spring and fall may indicate that infections of the respiratory tract are of little etiologic significance.



Seasonal incidence in 258 cases of appendicitis.

TABLE 2.—*Distribution of Cases by Months and Years*

	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
1925.....	1	0	2	1	4	4	4	4	5	1	2	2	30
1926.....	1	6	1	2	3	6	1	5	3	1	4	3	36
1927.....	0	1	3	3	1	5	3	5	4	0	1	0	26
1928.....	5	3	3	1	3	5	5	7	1	0	2	0	35
1929.....	2	1	4	6	2	2	3	6	1	1	5	1	34
1930.....	3	1	5	2	3	2	7	2	2	2	4	3	36
1931.....	0	1	3	2	1	2	6	5	2	1	2	1	26
1932.....	4	1	2	4	5	4	4	5	1	3	1	1	35
Total...	16	14	23	21	22	30	33	39	19	9	21	11	258
Per cent	6.1	5.4	8.9	8.1	8.5	11.6	12.7	15.1	7.3	3.4	8.1	4.1	99.3

ETIOLOGY

Bacteriology.—Appendicitis is an acute infectious disease which may be caused by a variety of organisms. Bacteriologic studies were made in only 42 cases in this series, the majority of cultures being obtained in cases of appendicitis with perforation. Pure culture of Bacillus coli was obtained in 26 cases. Scattered pure cultures of B. aerogenes, Staphylococcus and Streptococcus were obtained, and these organisms were also found mixed with B. coli in a few instances. In 9 cultures there was no growth. Although few of these cultures were made from

unperforated appendixes, the results closely approximate those reported by Warren,[6] who made cultures from various portions of the wall of the unruptured, acutely inflamed appendix—outside the mucous membrane. The majority of cultures showed B. coli.

Jennings[7] has drawn attention to the rôle of Bacillus Welchii in acute appendicitis and in peritonitis following perforation of the appendix. No anaerobic cultures were made in this series.

Many modifying factors have been suggested which have a bearing on the etiology of acute appendicitis. These may be classified as follows:

Previous inflammation of the appendix
Obstruction of the lumen
    (*a*) Foreign bodies
    (*b*) Worms
Acute infectious disease
    (*a*) Infection of upper respiratory tract
Gastro-enteritis
Dietary indiscretion
Abdominal trauma

Previous Inflammation of the Appendix.—A definite history of one or more previous attacks of acute appendicitis was recorded in 62, or 24 per cent, of the cases in this series. There were no fatalities in this group. As will appear later (table 4) this series of cases has been classified under three heads, depending on the extent of the disease. Of these recurrent cases, 50 were in group 1 (acute uncomplicated appendicitis), 8 in group 2 (acute appendicitis, ruptured, with local peritonitis) and 6 in group 3 (acute appendicitis, with general peritonitis).

Seventy-eight per cent of this group, therefore, were operated on before the infection spread beyond the appendix, as compared to only about 55 per cent for the whole series. This suggests two possible factors influencing the course of the disease. In the first place, the fact that 3 patients recovered spontaneously from a previous attack and that the present attack was mild suggests a greater general resistance to infection, whatever that may mean. In the second place, it is entirely possible that many of the patients had been put on the alert by the previous trouble and had sought medical aid sooner.

Obstruction of the Lumen.—(*a*) Foreign Bodies: Fecaliths were the only foreign bodies found in this series, and were reported in 38 of 258 cases. It is probable that fecal concretions occurred more frequently than were recorded. Though it cannot be proved by this study that the impaction of a fecalith actually precipitated the attack of acute

6. Warren, Shields: The Etiology of Acute Appendicitis, Am. J. Path. **1**:241 (March) 1925.

7. Jennings, J. E.: The Relationship of the Welch Bacillus to Appendicitis and Its Complications, Ann. Surg. **93**:828 (April) 1931.

appendicitis, the operative note in many instances suggests that the fecalith was a factor in the rupture of the appendix. It is striking that fecaliths were found in the three appendixes that ruptured in less than twenty-four hours after the onset of symptoms. This finding is in accord with the observations of Wilkie [8] on the importance of obstruction of the lumen by fecal concretion in the etiology of acute appendicitis.

(*b*) Worms: In 1913, 20.5 per cent of the children in a selected community served by this hospital were found to be infested with Ascaris lumbricoides.[9] Although this incidence has been greatly reduced, infestation is still fairly common. Despite the finding of Ascaris ova and worms in the stool and at operation in the intestine in a number of cases, no worms were found in the appendix in this series. Infestation with Oxyuris vermicularis is much less common in this district. However, in one instance these parasites were found within the lumen of the appendix. Although infestation with intestinal parasites is probably more frequent in children than in adults, from this study it appears to be a rare cause of acute appendicitis. Corroboration is found in the work of Suzuki [10] and of Gordon.[11]

Infectious Disease.—Acute tonsillitis immediately preceded the onset of acute appendicitis in 10 cases; in 2 cases the appendicitis quickly followed acute bronchitis, and acute appendicitis developed in 1 patient who was already in the hospital because of empyema of the pleura. In no other case in this group did appendicitis develop after a recognized preexisting condition.

Rosenow [12] presented evidence to indicate that appendicitis may be of hematogenous origin. On the other hand, Warren [6] was unable to confirm this idea. If there is any connection between infections of the throat and appendicitis, acute tonsillitis should be of more etiologic significance in children than in adults.

Gastro-Enteritis.—Attention has already been drawn to the higher incidence of acute appendicitis in children during those months when gastro-intestinal disorders are most frequent. Gastro-enteritis may be of etiologic significance, though no data are available from this study to confirm or to disprove this impression. Every surgeon has had experience with acute appendicitis following close on the heels of what

8. Wilkie, D. P. D.: The Etiology of Acute Appendicular Disease, Canad. M. A. J. **22**:314 (March) 1930.

9. Ann. Rep. Dept. Health Virginia, 1914, p. 98.

10. Suzuki, K.: The Rôle of Oxyuris Vermicularis in the Etiology of Appendicitis and Allied Pathological Conditions, Surg., Gynec. & Obst. **21**:702, 1915.

11. Gordon, H.: Appendiceal Oxyuriasis, Ann. Int. Med. **4**:1521 (June) 1931.

12. Rosenow, E. C.: The Bacteriology of Appendicitis and Its Production by Intravenous Injection of Streptococci and Colon Bacilli, J. Infect. Dis. **16**:240, 1915.

could be diagnosed only as gastro-enteritis, whether or not any infectious agent was shown.

Dietary Indiscretion.—Two patients in this group suffered an attack of acute appendicitis directly after overeating. Richter [2] mentioned 3 cases in a series of 172 in which dietary indiscretion was stressed in the history as initiating the attack. Since unwise eating, both as to amount and as to choice of food, is so common in children, it seems that if it were of etiologic significance such a history should be obtained more frequently.

Abdominal Trauma.—One patient in this group gave a history of having struck the lower portion of the abdomen on the corner of a table just prior to the onset of symptoms of appendicitis. The fact that no other patient gave a history of trauma suggests that this is rarely if ever a cause of appendicitis.

TABLE 3.—*Distribution of Pain at Onset and Frequency of Nausea and Vomiting*

Initial Symptom	Location of Pain at Onset	Number of Cases	Per Cent	Number of Cases in Which There Was	
				Nausea	Vomiting
Pain	Epigastrium	91	37.0	83	81
Pain	Right lower quadrant of abdomen	56	22.8	43	37
Pain	General over the abdomen	50	20.4	43	42
Pain	Lower portion of abdomen and about umbilicus	36	14.6	32	32
Pain	Left lower quadrant	4	1.6	3	2
Nausea and vomiting		8	3.2	8	8
Total		245	99.6	212	202
Not recorded in history		13			

SYMPTOMATOLOGY

The usual sequence of symptoms, namely, pain somewhere in the abdomen, followed by nausea and vomiting and localization of pain in the right lower quadrant, is so constant in acute appendicitis that it is generally accepted as the rule. Pain was the first symptom in 237, or 96.7 per cent, of the 245 cases in which the history was adequate. The location of pain at the onset is shown in table 3. That only 37 per cent of these children complained of epigastric pain at the onset is in striking contrast with the usual textbook picture of acute appendicitis.

Nausea occurred in 212 of these cases, or 86.5 per cent, and was followed by vomiting in 202, or 82.4 per cent. Nausea with vomiting was given as the initial symptom in 8 cases. The high frequency of nausea and vomiting may be due to the fact that children are prone to vomit.

Localization of pain at McBurney's point occurred in 94.6 per cent of the 149 cases in which an adequate history was given. Localization

of pain occurred in from one to twelve hours in 36.1 per cent of these cases; in from twelve to twenty-four hours in 42.4 per cent; in from twenty-four to forty-eight hours in 17 per cent, and in from two to four days in 4.9 per cent.

SIGNS

Tenderness over McBurney's point was present in all but 1 of 247 cases in which the preoperative physical findings were properly recorded. The 1 exception was the case of a 12 year old child, who had been sick twenty-four hours before admission. At the onset of illness, there was epigastric pain, followed by nausea and vomiting and localization of pain in the right lower quadrant. On examination, a deep-seated mass was felt low on the right, but there was no tenderness or muscle spasm. At operation an acutely inflamed appendix was found, wrapped in omentum, lying deep in the iliac fossa. The obvious explanation for this exception is the lack of peritoneal involvement.

Tenderness with spasm of the right rectus muscle was present in 78.9 per cent of the cases. In a few cases in which the appendix was retrocecal, these findings were present in the right flank. A tender mass in the right lower quadrant of the abdomen was the principal physical finding in 6 per cent of the cases.

LABORATORY DATA

The laboratory test of most importance is the white blood cell count. The preoperative white cell count was recorded in 234 cases. In the 127 cases in which the appendix had not ruptured, the counts ranged from 6,000 to 29,000 (average, 15,200). Eighteen counts were under 10,000. In 70 cases in which a ruptured appendix was associated with localized peritonitis, the counts ranged from 6,400 to 33,600 (average, 18,700) and only 3 counts were under 10,000. In the 37 cases in which the peritonitis was not localized the counts ranged from 5,000 to 30,000 (average, 19,000), and 3 were under 10,000. Preoperative differential counts, Schilling counts and determinations of the sedimentation rate were done so rarely in the acute cases that analysis of the scattered results is not worth while. Chamber differential counts were reported preoperatively in most of the histories, but these, although clinically useful, are not adequate for a statistical study.

MORTALITY

To facilitate analysis of this series from the point of view of mortality, the cases have been arbitrarily placed in three groups as shown in table 4. A series of cases in adults seen in this hospital has been similarly divided in order to compare the distribution of cases and the mortality in each group. In those cases in children in which the appen-

dix was not ruptured there were no deaths. However, peritoneal involvement is followed by a relatively high mortality. The mortality is particularly high when there is a failure to localize the infection of the peritoneum.

Although the size of the adult series is much larger than that of the children, the distribution of cases in each of the three groups is so nearly the same that the mortality figures may be compared. The mortality in groups 1 and 2 of both series of cases is practically the same. In group 3 the mortality of 34 per cent in children as compared to 16 per cent in the adult is strongly indicative of a much lower resistance to peritoneal involvement in the child.

TABLE 4.—*Distribution of Cases and Mortality in Each Group*

		Children				Adults			
Group	Distribution of Cases	No. of Cases	Per Cent	Deaths	Per Cent	No. of Cases	Per Cent	Deaths	Per Cent
1	Cases of acute appendicitis, not ruptured	142	55	0	0	1,447	62	11	0.7
2	Cases of acute appendicitis, ruptured, with localization of peritonitis or definite abscess formation	72	28	5	6.9	552	24	20	4.5
3	Cases of acute appendicitis, ruptured, with no localization of peritonitis	44	17	15	34.0	337	14	39	16.0
	Total	258	100	20	7.7	2,336	100	70	2.9

FACTORS INFLUENCING MORTALITY

From these figures at least three factors that influence these mortality rates can be detected. The importance of early diagnosis and surgical intervention has already been demonstrated in table 4. In 116 (45 per cent) of the children in this series the appendix had ruptured before operation. There is good reason to believe from the histories that no appendix ruptured after admission to the hospital. Peritonitis developing after rupture of the appendix is the most serious complication to be considered in acute appendicitis in children.

The second factor seems to be the duration of illness before admission, which is closely related, of course, to the extent of the disease (table 5). Only 45 patients were admitted to the hospital in less than twenty-four hours after the onset of symptons, which represents a small percentage of the entire series. Although the appendix was not ruptured in the majority of cases in which the patient was seen within the first forty-eight hours after the onset of symptoms, the 10 cases in which the appendix had ruptured in this interval emphasize the necessity of early removal.

A third factor in acute appendicitis is the use of cathartics (table 6). It is difficult to say whether or not catharsis will cause the rupture of an inflamed appendix or whether purgation after the rupture of an appendix will cause a spreading of the infection of the peritoneum. In 36 per cent of the histories in this series it was stated that one or more cathartics had been given prior to the patient's admission to the hospital. It is striking that there had been purgation in only 26 per cent of the cases in which the appendix did not rupture whereas it had been done in 47.5 per cent of those in which rupture occurred. The drugs most commonly used were castor oil, magnesium sulphate, mild mercurous chloride and "black draught" (an infusion of senna).

TABLE 5.—*Duration of Illness Before Admission*

	Duration of Illness Before Admission											
	0-12 Hours		12-24 Hours		24-48 Hours		48-72 Hours		After 72 Hours		Not Known	
Group	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
1.....	17	0	25	0	43	0	27	0	27	0	3	0
2.....	0	0	0	0	4	0	12	0	55	5	1	0
3.....	0	0	3	0	3	1	15	5	23	9	0	0
Total	17	0	28	0	50	1	54	5	105	14	4	0

TABLE 6.—*Number of Patients Receiving Cathartics* *

	Patients Not Receiving a Cathartic			Patients Receiving a Cathartic		
Group	Number	Deaths	Per Cent	Number	Deaths	Per Cent
1.....	106	0	0	36	0	0
2.....	22	1	3.1	40	4	10.0
3.....	28	11	39.3	16	5	31.2
Total.....	106	12	7.2	92	9	9.8

* Purgation was done in 47.5 per cent of the patients with a ruptured appendix and in 26 per cent of the patients with an unruptured appendix.

COMMENT

The evidence presented indicates that there is no essential difference between the clinical picture of acute appendicitis in the child and that in the adult. An analysis of this series of cases indicates that the etiology, history and physical findings are identical for all practical purposes. The main difference lies in the higher mortality rate in children.

The difference in mortality in the two series of cases here reported is particularly striking in view of the fact that the distribution of cases in the three groups is practically the same in the two age periods.

There are several factors that may indirectly contribute to the higher death rate in children. The omentum in the child hangs at a higher level than that in the adult, and is therefore less efficient in the walling off of an inflammatory process in the lower portion of the abdomen. This

fact may in part explain the lower resistance of the child to peritoneal involvement and, indirectly, the higher mortality. It is assumed by many surgeons that the thinness of the wall of the appendix in the child may permit earlier peritoneal involvement. This assumption is not supported by this study, since there were a large number of cases of acute inflammation of the appendix of more than forty-eight hours' duration without peritoneal involvement, and the incidence of peritonitis in children and in adults in the present series was about the same.

Difficulties in arriving at an early diagnosis may contribute to the mortality by delaying operation until after the appendix has ruptured. In spite of the fact that typical symptoms are present in the majority of cases, it is often difficult to obtain a complete history in younger children.

The figures presented here demonstrate that the more common physical findings are present in children as in adults, in the vast majority of cases. According to accepted opinion, the position of the appendix with reference to the abdominal wall determines the location of tenderness on physical examination. The records of the present series offer no evidence to confirm or dispute this opinion. In the individual case other findings than those noted may be of great significance, i. e., tenderness along the lower border of the liver, maximal tenderness and spasm in the right flank and tenderness or a mass on rectal examination. It must be noted that in the vast majority of cases the findings on which to base a diagnosis may be elicited early in the course of the attack.

Unfortunately gastro-intestinal disorders, described by the parents as "biliousness," "stomach ache" or constipation, which yield so promptly to some home remedy, usually a cathartic, are so frequent in children that appendicitis is not considered until the disease is well advanced and the diagnosis obvious. The supposed frequency of constipation as an accompaniment of appendicitis doubtless may contribute to the free use of cathartics. It should be the attitude of every physician and parent that each case of abdominal pain is a potential case of appendicitis and should be watched carefully and closely, laxatives and sedatives being withheld, until a diagnosis can be reached. In those few atypical cases in which this may not be possible, early exploration would be far safer than the risk of peritonitis following the rupture of the appendix. It must be emphasized that the incidence of perforation of the appendix in the present series is practically no larger than that found in the adult series. The greater mortality in children is undoubtedly due to the lower resistance of the child to peritoneal involvement, and prevention of this complication is of first importance in the reduction of the mortality.

SUMMARY

Two hundred and fifty-eight cases of acute appendicitis in children proved by operation have been reviewed. Certain outstanding findings have been emphasized. In this series the age distribution curve reached a peak at 12 years and remained high during the following two years. The results of this and similar studies indicate that there is a gradual increase in incidence from infancy to adult life, rather than a sharp increase at a given age period.

The greatest frequency of acute appendicitis in children was noted in the months of June, July and August. Since gastro-intestinal disorders are so common during the same period, such conditions may be of importance in the etiology of appendicitis.

A definite history of one or more previous attacks of acute appendicitis was noted in 64 of the cases in this series. The fact that 50 of the cases were in group 1 suggests greater resistance to infection and greater watchfulness on the part of the parents in subsequent attacks.

The general clinical picture of the disease in children was found to be similar to that in adults. Figures derived from this series of cases have been compared with figures drawn from a series of cases in adults seen in this clinic. The distribution of cases into three groups, namely, (1) acute appendicitis, not ruptured, (2) acute appendicitis, ruptured, with localization of peritonitis or definite abscess formation, and (3) acute appendicitis, ruptured, with no localization of peritonitis, was essentially the same in the two age periods. The mortality in groups 1 and 2 was essentially the same in the two series, but in group 3 the mortality in the children was 34 per cent as compared to 16 per cent in the adults. This high figure in group 3 in children accounts largely for the difference in total mortality, 7.75 per cent in children and 2.9 per cent in adults.

It appears from this study that the high mortality in children is due to the lower resistance to peritoneal involvement. It is obvious that reduction in mortality can best be accomplished by early diagnosis and removal of the appendix before involvement of the peritoneum occurs.

THERAPEUTIC USE OF CONCENTRATED STREPTOCOCCUS SERUM OF NEW YORK STATE DEPARTMENT OF HEALTH

IN INFECTED WOUNDS

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NEW YORK

In our series of twenty-six patients treated with the concentrated streptococcus serum of the laboratory of the New York State Department of Health, there are thirteen with infections which would ordinarily be classed in the field of general surgery. In six, the infection began in the hand. In three patients, the lesion was apparently induced by pressure or by accidental laceration, and in four streptococcic infection appeared after surgical operation. Of the thirteen patients, eight survived and five died.

INFECTIONS OF THE HANDS

Streptococcic infection of the hand or its digits is rather frequent in physicians, nurses and laboratory personnel in hospitals. It is often trivial, but sometimes tragic, and there is good reason to believe that early neglect or unwise treatment in the early stage of the infection may sometimes contribute to the later unfortunate course. On the other hand, a fortunate outcome with early recovery does not of itself prove the efficacy of the treatment followed except for that particular case. In the present series we have six patients with such infection of the hand.

CASE 1.—M. E., a youth, aged 19, a volunteer worker in the pathologic laboratory, noticed a small irritated abrasion on the hypothenar eminence of the right palm about March 6, 1933. He applied iodine. In the next two days the region became swollen and tender and discharged a small amount of pus. A

This work was made possible by a grant from the Josiah Macy Jr. Foundation.

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The patients whose records are utilized in this paper were treated in the clinical services of the following physicians: Dr. R. F. Carter, Dr. T. H. Cherry, Dr. J. F. Erdmann, Dr. C. M. Gratz, Dr. C. G. Heyd, Dr. A. A. Levy, Dr. H. Lynch, Dr. J. J. Moorhead, Dr. H. H. Ritter and Dr. J. E. Sheehan.

culture showed hemolytic streptococci. An ampule of 20,000 units of the concentrated streptococcus serum was injected subcutaneously into both arms. On the following day there was marked swelling about the sites of injection of the serum with an urticarial eruption extending from the shoulder to the wrist on both arms. This disappeared after two days, and the original lesion healed promptly. The patient regards the infected abrasion as a trivial affair but retains a vivid and unpleasant recollection of the serum sickness.

Case 2.—I. N., a student nurse, aged 20, had cellulitis of the left hand early in January. This was incised, and she was admitted to the hospital as a patient from January 6 to 10. After returning to duty for five days, she was again admitted to the hospital with a temperature of 102.6 F. On January 24 a large abscess in the left axilla and another on the right side of the neck were opened. The pus from these contained streptococci, although the original lesion of the hand contained both staphylococci and streptococci. After the drainage on January 24, the patient received 40,000 units of the concentrated streptococcus serum on January 25 and an equal amount on January 26. She was discharged on February 11. The result was highly satisfactory. Her abridged clinical chart has been presented eleswhere,[1] as this case was selected as an example of this group used in a previous paper.

Case 3.—M. D., a graduate nurse, while attending a patient in whom an infection developed following an operation, acquired an inflammation about the nail of the right ring finger on Aug. 9, 1933. After a culture was taken, 0.5 cc. of asparagine staphylococcus bacteriophage was injected into the tissues of the distal phalanx on August 11. The finger was kept moist and warm as far as the patient's duties would permit. It was deemed unnecessary for her to give up her service, and she continued on active nursing duty. On the following day the culture showed hemolytic streptococci predominating, and the finger was still swollen and tender. After an intracutaneous test at 8:43 a. m., which revealed no hypersensitiveness to horse serum, a second dose of 0.5 cc. of the concentrated streptococcus serum was given subcutaneously at 9 a. m., and at 9:15 a. m. the remainder of the ampule was given intravenously, the total amount in the three doses being 20,000 units. Improvement was distinctly evident the next morning, and in two more days the finger appeared to be normal. The patient remained on duty regularly. There was no untoward reaction, nor was there any serum sickness.

Case 4.—R. M., a physician, aged 38, had an inflammation of the index finger on his left hand, apparently due to infection acquired in performing an autopsy. After forty-eight hours, he appeared for duty on Monday morning, Jan. 9, 1933, with signs of a severe infection. The finger was quite swollen, and there were visible red lines extending up the forearm and a painful swelling in the axilla. He was at once admitted to the hospital and put to bed. Microscopic examination and cultures of the exudate from the finger taken on the preceding Saturday showed predominant staphylococci.

The abridged clinical record is shown in chart 1. On January 9 experimental staphylococcus antitoxin was given in three doses to insure desensitization, and 1 cc. of staphylococcus bacteriophage was injected subcutaneously into the left arm near the axilla. On the next day our concern seemed rather ridiculous, but on January 11 the pain and swelling in the axilla had increased, and therefore further injections of staphylococcus bacteriophage were given subcutaneously

1. MacNeal, W. J.: Specific Treatment of Septic Infections, Particularly with the Aid of Bacteriophages, Am. J. M. Sc. **187**:623 (May) 1934.

near the axilla on January 11 and 12. On January 13 a circumscribed deep axillary abscess was recognized, and on the next day, under ethylene-oxygen anesthesia, this was conservatively opened, and the major portion of the nail of the index finger was cut away. Microscopic examination of the axillary pus revealed definite chains of cocci, and the cultures subsequently gave a pure growth of hemolytic streptococci. Without awaiting the result of this culture, the patient was at once treated for the streptococcus infection. A blood culture was taken, which remained sterile. Two ampules, 40,000 units, of the concentrated streptococcus serum were given subcutaneously, and this dose was repeated on January 15. A distressing general urticaria with moderate laryngeal edema appeared on the evening of January 16, disappearing in twenty-four hours. The patient was discharged on January 19 and returned to duty on January 23.

This is the fourth instance of cellulitis of the hand and axillary adenitis observed in our staff as a result of infection contracted at autopsies in a period of twenty-two years. In the other three the period of hospitalization was a matter of months, and the final fortunate outcome seemed for a time doubtful. This fourth case in the series is the first one in which specific bacteriotherapeutic measures were employed.

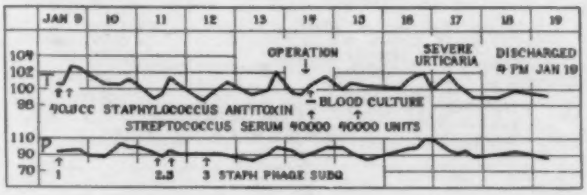


Chart 1.—Abridged clinical record of R. M., a man, aged 38. In this patient cellulitis of the left hand developed, apparently due to infection acquired in performing an autopsy. The patient was treated for infection with the staphylococcus until January 14, when incision of an axillary abscess revealed numerous streptococci. Streptococcus serum was given subcutaneously on January 14 and 15. Severe serum sickness developed on January 16. The patient was discharged on January 19 and returned to duty on January 23.

Case 5.—M. R., a Negress, aged 46, employed in washing glassware in the laboratory, had an inflammation about the nail which developed after she pricked her right middle finger with a pin in the back of her apron on Feb. 18, 1933. On Sunday, February 19, the finger became increasingly painful and swollen. A slight fever, not accurately recorded, was present. On February 20 the finger was swollen for half its length, and the axillary nodes were enlarged. The swelling was most marked about the nail. This was punctured with a small sterile needle, and a small amount of blood-tinged pus was obtained. Microscopic examination revealed streptococci, and cultures gave colonies of hemolytic streptococci, Staphylococcus albus and colon bacilli of the aerogenic type. On February 20 a subcutaneous dose of 20,000 units of the concentrated streptococcus serum was given, and on February 25 the lesion on the finger was irrigated with coli bacteriophage. Progress was satisfactory. The patient was absent from duty only a half day, Monday afternoon, February 20. Her occupation, namely, washing laboratory glassware in warm water, may have contributed to the prompt recovery.

Case 6.—J. H., a man, aged 46, received a puncture wound from a piece of wire beneath the nail of his right thumb on July 8, 1933. Several hours later the thumb became swollen and painful, and there were red streaks along the forearm, with soreness at the elbow and the axilla. On the day of admission to the hospital there had been several chills and a high fever. The patient came to the hospital at 6:30 p. m. on July 10. At this time the right thumb was swollen, and its distal third was yellow and without feeling. The entire hand was swollen, and there was a large prominence in the anterior interosseous region of the forearm. The right epitrochlear and axillary nodes were enlarged. The temperature was 106.2 F.

The abridged clinical record is shown in chart 2. Immediate operation revealed only a minute quantity of exudate at the tip of the thumb, but there was a large amount of pus at the thenar eminence. Gas bubbles were observed beneath the skin. Immediately after the operation there was a severe chill followed by a lowered temperature. Again on July 11 there was a chill lasting ten minutes. The patient began to cough and also to suffer from persistent attacks of hiccupping, which continued throughout most of his illness.

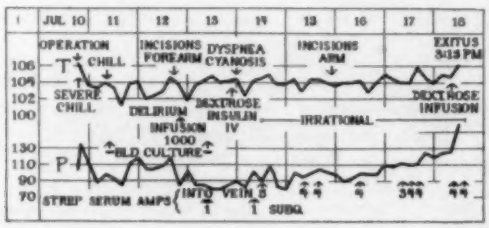


Chart 2.—Abridged clinical record of J. H., a man, aged 46. This patient had cellulitis of the hand and forearm following puncture of the right thumb. There was a mixed infection in which hemolytic streptococci were abundant. There were, however, also gas bubbles beneath the skin. Streptococcus serum was given on July 13, 14, 15, 16, 17 and 18, the total amount being 38 ampules, or 760,000 units. The forearm was incised on July 12, and the upper part of the arm was incised on July 15. The patient died on July 18. At autopsy, the streptococcus seemed to have played a minor rôle in the terminal stages of the disease.

Cultures of the pus obtained on July 10 yielded only hemolytic streptococci on the blood agar plates and in a test tube two-thirds full of dextrose meat infusion agar, and in litmus milk there was no evidence of growth of Clostridium Welchii. In blood broth, however, a slender gram-positive rod, evidently anaerobic, was found along with the streptococci and diphtheroid bacilli. Blood cultures taken on July 11 and 13 remained negative.

On July 12 the right arm was red and swollen to the axilla. At 5:30 p. m. on this day, multiple incisions were made in the forearm, and an abscess cavity was found above the annular ligament of the wrist and another in the upper third of the forearm. The patient was now delirious and remained irrational most of the time thereafter. He received several infusions of dextrose. On the evening of July 15, multiple incisions were made in the arm between the elbow and the axilla, and further incisions were made in the forearm. The cough became worse, and the patient raised mucus containing abundant small gram-negative rods, apparently Pfeiffer's bacilli.

The concentrated streptococcus serum was given first on July 13, one ampule of 20,000 units, in divided doses to insure desensitization. The same amount was given subcutaneously on July 14, and this was followed, after consultation with Dr. Maillard of the state laboratory, by massive intravenous doses, five ampules (100,000 units) at noon on July 14, eight ampules on July 15, four on July 16, eleven on July 17 and eight on July 18, the total serum given amounting to 38 ampules, or 760,000 units. The patient died on July 18.

Autopsy, performed five hours after death, disclosed purulent collections in the right elbow and shoulder joints, in addition to extensive dissecting purulent and emphysematous inflammation of the entire extremity, and bilateral lobular pneumonia. Pus from the shoulder joint yielded a few colonies of hemolytic streptococci; the predominant bacteria in cultures were green streptococci and diphtheroids. Anaerobic cultures yielded a slender gram-positive bacillus, not identified, and a few colonies of Cl. Welchii. Cultures of the heart's blood yielded only colonies of Streptococcus viridans. Apparently the activity of the hemolytic streptococcus in the mixed infection had been somewhat restricted by the serum but not completely suppressed.

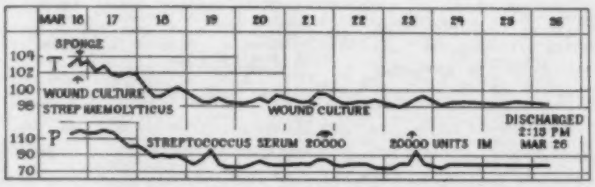


Chart 3.—Abridged clinical record of S. Y., a girl, aged 18. This patient had an accidental wound of the left cheek, which was heavily infected with streptococci. She received serum on March 21 and 23, with prompt local improvement.

ACCIDENTAL WOUNDS AND ULCERS DUE TO PRESSURE

In this subgroup there are three patients. One was the victim of an automobile accident, and the other two had infected ulcers caused by pressure. Two recovered and one died. None of them had a positive blood culture.

Case 7.—S. Y., aged 18, the daughter of a physician, suffered a contused laceration of the left side of her face in a motor accident on March 14, 1933. A wound about 3 cm. in length was closed by eight sutures. Bleeding from the nose persisted for twenty-four hours, and on March 15 the temperature ranged from 102 to 103 F. She was admitted to the New York Post-Graduate Hospital on March 16, with marked swelling of the face and a temperature of 102.8 F. Two stitches were removed, and a drain was inserted in the wound. Culture taken at this time yielded abundant hemolytic streptococci. The abridged clinical record is shown in chart 3. On March 17 all the remaining stitches were removed. Drainage was abundant. Roentgenologic study revealed no evidence of fracture, but did reveal evidence of inflammation in the right antrum as well as of the soft tissues of the face. The condition was not considered dangerous, but the patient's father as well as the attending surgeon in the case requested the aid

of specific bacteriotherapy on March 21. After a culture was taken, which later showed hemolytic streptococci, the patient was given an ampule (20,000 units) of the concentrated streptococcus serum in divided doses to insure densitization on March 21, and the same amount was given in a single intramuscular injection on March 23. The drainage from the wound diminished promptly and ceased entirely on March 25. The patient was discharged on March 26 with a granulating wound in a satisfactory stage of healing.

Case 8.—E. H., a woman, aged 37, had been under observation and treatment at the New York Post-Graduate Hospital for congenital dislocation and deformity of the left hip since Oct. 31, 1931. There had been three open surgical operations on the hip. The first two operations were performed in Europe in 1904 and 1921, respectively. After 1921 the patient had good function until March 1931, when she fell and hurt herself so that she was unable to walk for seven weeks. Again, about September 14, she fell and injured this hip and was

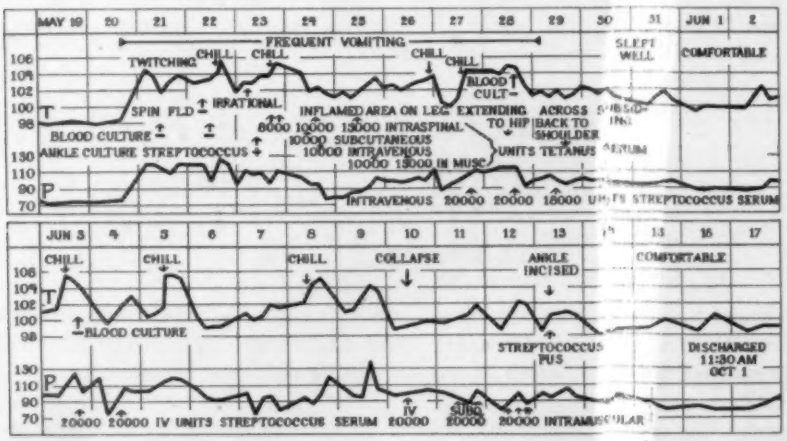


Chart 4.—Abridged clinical record of E. H., a woman, aged 37. Inflammation developed in the patient's leg, apparently due to pressure of a surgical dressing on May 20. A clinical diagnosis of tetanus led to the administration of tetanus serum, 33,000 units into the spinal canal, 10,000 units subcutaneously, 10,000 units intravenously and 25,000 units by intramuscular injection from May 24 to 26. An eruption diagnosed as erysipelas appeared on May 24. A blood culture remained negative. Streptococcus serum was given intravenously on May 27, 28 and 29, a total of 58,000 units. Prompt improvement followed this. On June 3, however, there was a chill, and streptococcus serum was given on this day and also on June 4, the total amount being 40,000 units. After an interval of five days a dose of 20,000 units of serum was given intravenously on June 10. A severe shock followed, evidently due to the serum. Divided subcutaneous doses were given on June 11, and divided intramuscular doses on June 12. The patient was discharged on October 1 in good condition.

not able to walk after that. The third operation at the New York Post-Graduate Hospital resulted in fixation by a bone graft, and following this the patient was discharged on Feb. 27, 1932, with a mechanical brace on the left lower extremity from the pelvis to the ankle. On March 9 the left ankle became swollen and

painful, and she noticed a small blister on it, which later became an ulcer. She came back to the hospital on March 13, and a course of light therapy, massage and electrical stimulation was instituted and continued to May 19. On the evening of May 20 the patient began vomiting and had a sharp rise in temperature and pulse rate.

Her abridged record after May 19 is shown in chart 4. She complained of severe pains in the hips, abdomen, back and head. Blood culture taken on May 21 remained negative, as did also subsequent blood cultures taken on May 22 and 28 and on June 3. On May 22 there was a chill lasting fifteen minutes, with stiffness of the neck, tremors of the mouth and jaw and arching of the back. Spinal tap yielded a normal spinal fluid. On May 23 the patient was irrational. Culture taken from the ulcer on the ankle showed hemolytic streptococci and Staph. albus. During the four days, from May 23 to 26, antitetanic serum, 33,000 units, was injected into the spinal canal, 10,000 units subcutaneously, 10,000 units intravenously and 25,000 units intramuscularly. Meanwhile the bacteriologic search for the tetanus bacillus by anaerobic culture methods and inoculation of animals gave negative results. The inflamed area on the ankle extended up the leg, reaching the region of the hip on May 28 and across the back to the level of the shoulder on May 29, after which it subsided. The concentrated streptococcus serum was given by intravenous injection, 20,000 units on May 27, the same dose on May 28 and 18,000 units on May 29. Clinical improvement was prompt. However, there was a chill and sharp rise in temperature on June 3; an intravenous dose of 20,000 units was given on this day and repeated on June 4. On June 8 there was increased pain in the left ankle and leg, and a chill with a rise in temperature to 105.2 F. On June 10 an intravenous injection of 20,000 units of the streptococcus serum was given, the interval after the previous dose having been six days. Two minutes later rigor and vomiting developed, and the pulse became imperceptible. Epinephrine was administered, and the collapse was relieved in about half an hour. On June 11 the same amount of serum was given in six subcutaneous doses without untoward effect, and on June 12 the same amount was given in four intramuscular injections without recognizable reaction. On June 13 the evidence of inflammation had disappeared except over the anterior aspect of the left ankle. This region was now incised and pus evacuated. Cultures of this pus yielded only hemolytic streptococci. Subsequent progress was satisfactory. The patient was kept under observation in the hospital until October 1.

Case 9.—P. H., a man, aged 62, was admitted to the hospital on Feb. 16, 1933, with a painful ulcer on his left foot. In June 1929 he had a sore on the dorsal surface of his right great toe which healed after several weeks. The present ulcer on the other foot appeared about Jan. 12, 1933, and had gradually extended. Since February 2 the patient had been confined to bed. Mild diabetes had been recognized for ten years, and insulin had been used occasionally. The urine had usually been sugar-free in recent years.

The abridged clinical record is shown in chart 5. The ulcer was excised on February 16, and on February 18 the second and third metatarsal bones were opened and purulent osteomyelitis found. This operation was followed by a chill, but blood culture taken at this time remained negative. Culture from the wound revealed the hemolytic streptococcus, colon bacillus and staphylococcus. Bacteriophages active against the colon bacillus and against staphylococcus were applied to the wound; 30 cc. of staphylococcus antitoxin was given subcutaneously on February 19 and 1 cc. of staphylococcus bacteriophage intravenously. On this same day

40,000 units of the concentrated streptococcus serum was given subcutaneously in three doses. With continuation of this treatment the general condition improved so that the patient was allowed out of bed on February 22 and 23 and was able to act on some important papers sent in from his office. On February 24 an amputation was performed at the middle part of the left thigh, immediately following a transfusion of 340 cc. The patient did not rally from this operation.

INFECTED SURGICAL WOUNDS

In this subgroup there are four patients: a girl of 19 with staphylococcic osteomyelitis, secondarily infected with the hemolytic streptococcus; a man 30 years old with streptococcic infection following operation for inguinal hernia; a man 47 years old, in whom general sepsis developed after excision of the inguinal lymph nodes, and a woman of 60 years, who likewise suffered from general sepsis following operation on a proctocele and hemorrhoids. Three died and one survived.

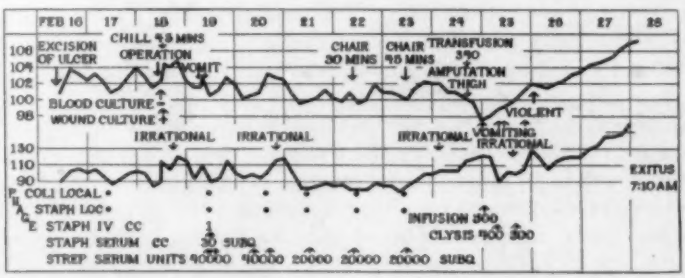


Chart 5.—Abridged clinical record of P. H., a man, aged 62. The patient had an ulcer on the dorsum of his left foot which extended to produce osteomyelitis of the metatarsal bones. Surgical excision and incision was supplemented by application of bacteriophage and the injection of streptococcus serum. A total of 140,000 units of streptococcus serum was given from February 19 to 23. The patient appeared somewhat improved. On February 24 the extremity was amputated in the region of the midthigh, after which the patient did badly and died on February 28.

Case 10.—M. H., a school girl, aged 19, was admitted to the hospital on Jan. 19, 1933, with osteomyelitis of the right ilium which involved the hip joint and an infection of the blood stream with Staph. aureus. Her abridged clinical record has been presented in an earlier paper from this laboratory.[1] She survived about four months. During this time the septicemia was overcome, but the operative wound became secondarily infected with various organisms, among which the hemolytic streptococcus seemed for a time to be the most dangerous. Large doses of the concentrated streptococcus serum were given on two occasions with favorable effect on the streptococcic infection. However, the patient continued to lose weight and, after various complications, aspiration pneumonia developed, and death occurred on May 17, 1933.

Case 11.—C. J. R., a man, aged 30, entered the hospital on Jan. 30, 1933, for relief of inguinal hernia which was ascribed to the effort of heavy lifting seven

weeks earlier. The abridged clinical record is shown in chart 6. A bilateral herniotomy was performed on January 31. The postoperative course was unsatisfactory, and on February 6 there was marked inflammation of the abdominal wall near the left incision, and pus was exuding from the incision. On February 7 the inflamed area was incised, and a culture of the exudate was taken. This yielded a growth of the hemolytic streptococcus. A transfusion was given on February 9 and, on the next day, multiple incisions were made in the abdominal wall. On February 14 the aid of bacteriotherapeutic measures was requested, and after a blood culture was taken, the concentrated streptococcus serum was administered, 20,000 units in three doses. The serum was continued on February 15, but after 5,000 units it was discontinued by order of the attending surgeon, who preferred to place his faith in other measures. A transfusion of 600 cc. was given on February 16. On February 17 the left seventh rib was resected, and the pleural cavity was opened. A small amount of sterile watery fluid containing cholesterol crystals was obtained. A blood culture taken on February 18 gave

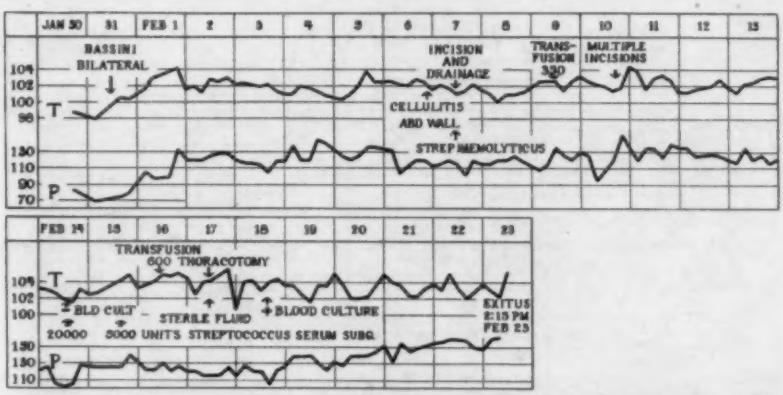


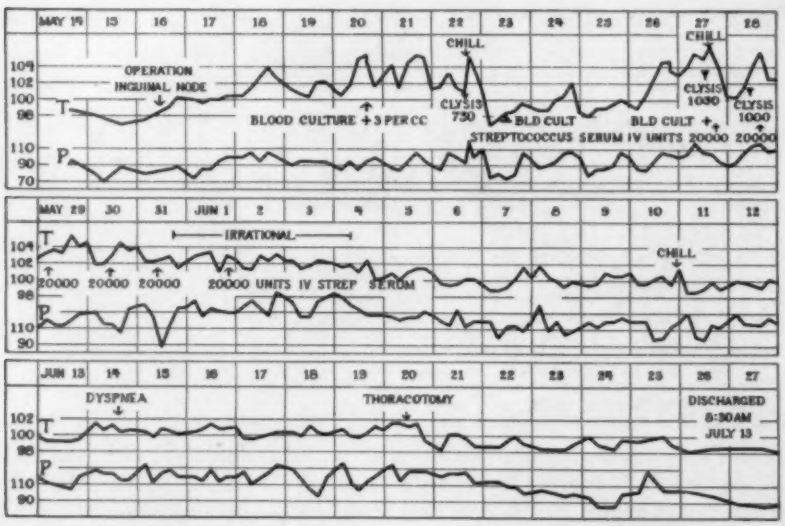
Chart 6.—Abridged clinical record of C. J. R., a man, aged 30. The patient was operated on for relief of bilateral inguinal hernia on January 31. Postoperative inflammation due to hemolytic streptococci was recognized on February 6. This was treated by transfusion and by multiple incisions. Streptococcus serum was started on February 14 and discontinued on February 15 after 25,000 units had been given. Transfusion of 600 cc. was performed on February 16, and a rib resection was done on February 17. On the next day a positive blood culture was obtained, the organism being a hemolytic streptococcus. The patient died on February 23.

a positive growth of hemolytic streptococci. On this day evidence of thrombophlebitis appeared in the left leg, and this condition progressed rapidly. The patient died on February 23.

CASE 12.—L. G., a man, aged 47, was admitted to the hospital on Feb. 20, 1932. In the latter part of January swellings developed in both inguinal regions, and on February 9 the patient's physician incised the right inguinal abscess and evacuated a quantity of pus. On admission to the hospital a draining sinus was present on this side, and there was inflammatory enlargement of the left inguinal nodes. On February 29 specimens were taken for biopsy from the right and left inguinal regions. These revealed a chronic purulent lymphadenitis without evidence of

tuberculosis. Pus taken at the same time from the right inguinal region failed to give any growth in dextrose broth and blood agar plates. These culture methods could hardly be expected to bring to development a possible bacillus of Ducrey but would seem adequate for the hemolytic streptococcus. The patient was discharged on March 8.

On May 14 he was again admitted to the hospital with continuing inguinal adenitis and a persistent small sinus in the right inguinal scar. The abridged clinical record from this date is shown in chart 7. On May 16 the old surgical scar in the right groin together with the underlying lymph nodes was excised. The microscopic study of this specimen disclosed a chronic purulent inflammation. Culture was not made. On May 18 the temperature rose to 104 F. Blood culture taken on May 20 revealed three colonies of hemolytic streptococci per cubic centimeter of blood. Clysis of 750 cc. on May 22 was followed by chill and a rise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6:30 AM
JULY 13

Chart 7.—Abridged clinical record of L. G., a man, aged 47. Bilateral inguinal adenopathy developed in January 1932, and a right inguinal abscess was incised on February 9. On May 16 a persistent sinus and the lymph nodes in the right inguinal region were excised. On May 20 blood culture yielded streptococci. Streptococcus serum was administered intravenously on May 27, 28, 29, 30 and 31 and June 1, a total of 120,000 units. The patient did well for a time, but on June 20 an exudate in the chest was evacuated by rib resection. He was discharged July 13 in good condition.

in temperature to 105.2 F. Blood culture taken on May 23, when the temperature was low, remained sterile. However, on May 27 a blood culture was taken which became positive for hemolytic streptococci. On this day the temperature reached 106.6 F. after a clysis of 10 per cent dextrose. At 6:30 p. m. the patient was given 20,000 units of the concentrated streptococcus serum intravenously, and this dose was repeated daily to June 1. Severe pain in the chest and labored breathing appeared on May 29, and on June 1 the cough raised some clotted blood as well as thick mucus. The patient was irrational much of the time from May 31 to June 4.

Therapeutic efforts, aside from the injections of serum, were discontinued after May 28. The patient gradually improved until June 10, when he complained of pain in the chest, and at night there was a chill lasting ten minutes. On June 15 there was dulness everywhere below the scapula on the right side of the thorax, and the signs of pleural exudate were confirmed by roentgenographic examination on June 18. On June 20, under local anesthesia, a thoracotomy evacuated pus under pressure occupying the entire right pleural cavity. Culture of the pus revealed abundant Pfeiffer bacilli and a few colonies of hemolytic streptococci. The postoperative course was satisfactory. The patient was allowed to be up in a chair on June 30; he walked on July 11, and was discharged with his wounds healed on July 13. There was no serum reaction in this case.

Case 13.—S. H., a woman, aged 60, was admitted to the hospital on May 2, 1932. Her abridged clinical record is shown in chart 8. On May 4, under nitrogen monoxide and ether anesthesia, operations for internal hemorrhoids and for proctocele were performed. On May 6 bleeding from the vaginal wound was con-

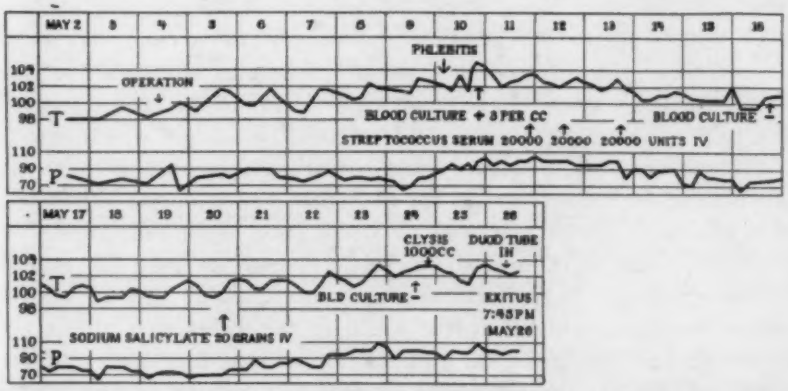

Chart 8.—Abridged clinical record of S. H., a woman, aged 60. This patient had a perineal operation and hemorrhoidectomy on May 4. On May 9 thrombophlebitis developed in the left thigh, and a positive blood culture was obtained on May 10. The serum was given intravenously on May 11, 12 and 13, a total of 60,000 units, followed by marked improvement. However, the condition became worse again on May 19. Sodium salicylate was given intravenously on May 20. The patient died on May 26.

trolled by packing. The temperature continued to mount gradually. On the night of May 9 severe pain developed along the inner side of the left thigh, and by morning of May 10 there was definite tenderness along the femoral vein. The temperature rose to 105 F., and petechiae appeared over the body. A blood culture taken that evening yielded three colonies of hemolytic streptococci per cubic centimeter of blood. The concentrated streptococcus serum was given intravenously, 20,000 units each on May 11, 12 and 13. The temperature response was satisfactory, and a blood culture taken on May 16, as well as one on May 24, was negative. However, on May 13 the urine showed some protein (one plus) and a considerable number of leukocytes as well as granular casts. Culture of the urine was not undertaken. On May 20 there was moderate vaginal bleeding, and there was edema of the left buttock and an inflamed area in the left inguinal region.

An intravenous dose of 20 grains (1.3 Gm.) of sodium salicylate was given on this day. On the next day the area of inflammation had extended, and the patient became mentally confused. Vaginal bleeding continued. There was no evidence of serum disease. The patient died on May 26. Postmortem examination was not permitted.

COMMENT

In these thirteen patients making up a somewhat heterogeneous group there were eight survivors and five who died. Six of the patients had infections of the hand, the impending gravity of which cannot be accurately estimated in advance. The lesions when first seen were of such a nature that surgical incision for drainage would have been the treatment of choice in our hospital only a few years ago. Three of these patients were treated without incision by bacteriotherapeutic measures in which the concentrated antistreptococcus serum of the laboratory of the New York State Department of Health was evidently the important factor. Warmth and moisture were employed locally. In these three the threatening disorder proved to be trivial. In two of the patients, a nurse, I. N., and a physician, R. M., the serum was given only after surgical incision of an axillary abscess which revealed the streptococcus. The recovery was surprisingly prompt in both. The sixth patient of this group, J. H., obviously had a mixed infection in which anaerobic bacteria as well as streptococci were concerned. His thumb and hand were incised on July 10, and on July 12, multiple incisions were made in the wrist and forearm; again on July 15, multiple incisions were made in the forearm and in the upper part of the arm. The serum was first given on July 13, and it was increased to a total amount of 760,000 units without success. However, at the autopsy it appeared that the dangerous hemolytic streptococcus, so abundant in the original wound, had not played the important rôle in the fatal outcome.

As a result of our experience we have become somewhat more conservative in the matter of incising infected fingers. Exudate is needed for microscopic examination and culture, but when these examinations are inconclusive or even while their outcome is being awaited, we favor the use of prophylactic bacteriotherapeutic measures and especially the streptococcus serum. We do not wish to suggest that surgical incision of infected fingers and hands should never be undertaken, but we do believe that the early use of serum against streptococcic infection will often suffice to limit the extension of the disease and to avoid serious deformity. It is perhaps not too much to hope that the disabling scar contractures, the long weeks of hospitalization and the occasional tragic fatality following streptococcic infection of the hands, especially in physicians and nurses, may be ameliorated by the early administration of a potent antistreptococcus serum. Even when incisions are made, we are convinced that the streptococcus serum, as exemplified by the

concentrated serum of the New York State Department of Health, offers an important aid in further combat against the infection.

In the one patient with a recently inflicted gash in the face resulting from a motor accident, a threatening streptococcic infection rapidly subsided after the administration of the serum, a matter of some importance in relation to scar formation, particularly on the face of a young woman.

The two patients with ulceration on the lower extremity responded favorably to treatment with the streptococcus serum. In one of these, E. H., there is an emphatic illustration of the danger sometimes encountered in giving horse serum intravenously. This patient received the concentrated streptococcus serum on May 27 and 29 and on June 3 and 4. Then after an interval of six days she received an intravenous injection of 20,000 units of the same serum. Severe shock appeared in two minutes, and the alarming condition persisted for half an hour. We have had opportunity to observe similar reactions of hypersensitiveness, so far without a fatal result, in several other patients, particularly when there has been a considerable interval between the successive doses of this serum, and we therefore urge extreme care in desensitization in all such cases. The outcome in this particular patient was fortunate. Without the serum she would probably have succumbed. The other patient, P. H., with ulcer of the foot, responded well to the bacteriotherapeutic measures, which were then discontinued in favor of a radical operative procedure with unfortunate outcome.

In the group of four patients with postoperative infections, the streptococcus serum accomplished, in our opinion, all that could reasonably have been expected of it. In M. H. the serum was resorted to with success on two occasions when a progressive streptococcic infection seemed otherwise uncontrollable. The eventual death of the patient took place without recognizable activity of the hemolytic streptococcus. The second patient, C. J. R., with extensive cellulitis of the abdominal wall, received only 25,000 units of the serum. Three days later, after a thoracotomy, the streptococcus had invaded the blood stream and the process became progressively worse until death on February 23, further serum treatment not being permitted. The third patient, L. G., affords an excellent contrast. After two positive blood cultures and a rise in temperature to 106.6 F. on May 27, this patient was given 120,000 units of the serum intravenously in six days with satisfactory effect. Following a thoracotomy on June 20 the patient made a rapid convalescence. The fourth patient, S. H., after a positive blood culture on May 10, received 60,000 units of the serum intravenously, with evident favorable effect. Serum was then discontinued. Death occurred on May 26.

It may be superfluous to state that these patients were, as a rule, not under our control, but were seen in consultation. In some instances, particularly when the outlook appeared most grave, the serum treatment was willingly accepted. Sometimes the administration of the serum was later interrupted. We think that further serum therapy would have been helpful in some of these instances.

SUMMARY AND CONCLUSIONS

1. Thirteen patients with conditions ordinarily classified in the field of general surgery, infected with hemolytic streptococci, were treated with the concentrated streptococcus serum of the laboratory of the New York State Department of Health. Eight survived and five died.

2. In one patient after the serum therapy had been discontinued streptococcic septicemia developed and death occurred. Two patients were treated with serum after positive blood cultures were obtained, and in both the blood became sterile. One of these recovered.

3. The serum is strongly recommended for infection of the hand in physicians, nurses and laboratory personnel, a type of lesion with dangerous possibilities when infected with hemolytic streptococci.

4. In accidental and in operative wounds, streptococcic infection should be treated with streptococcus serum.

5. Care should be exercised in the desensitization of patients who may be hypersensitive to horse serum.